

**PARTICLES CONTAINING AGRICULTURAL  
ACTIVE INGREDIENTS**

This continuation-in-part application claims the  
5 benefit of priority of U.S. Patent Application Serial No.  
09/104,565<sup>ABO</sup> filed June 25, 1998; which is a continuation of  
provisional application No. 60/051,285 filed June 30, 1997.

**BACKGROUND OF THE INVENTION**

This invention relates to compositions and methods for  
10 controlled release of agricultural chemicals.

An agricultural chemical, such as a biocide, a  
chemical hybridizing agent, or a plant growth regulator is  
applied to a plant, to a seed, or to soil at the beginning  
of a growing season and must maintain their effectiveness  
15 throughout the growing season, which can last for several  
months. However, the agricultural chemical may be degraded  
by chemical or biological processes and removed by wind or  
water from the site of application. As a result, it is  
necessary to apply high rates of the agricultural chemical  
20 to maintain the desired effect over time or to apply the  
chemical repeatedly during the growing season. However,  
high rates of certain agricultural chemicals can be  
phytotoxic to a plant which is sought to be protected  
("agronomic plant") from the disease or pest which the  
25 agricultural chemical is meant to control. For example,  
many fungicides, such as triazole fungicides, can be  
phytotoxic to the agronomic plant when applied in amounts  
that are necessary to provide agronomically adequate  
disease control.

0033014-060490

MAI  
s Numerous triazole fungicides have been developed and commercialized. The triazole fungicides are generally characterized as having a 1H-1,2,4-triazole group. Some individual representative triazole fungicides are listed in the table below.

Triazole Fungicide	CAS Registry Number
bitertanol	70585-36-3
bromuconazole	116255-48-2
cyproconazole	94361-06-5
difenoconazole	119446-68-3
epoxiconazole	106325-08-0
fenbuconazole	114369-43-6
fluquinconazole	136426-54-5
flusilazole	85509-19-9
flutriafol	76674-21-0
hexaconazole	79983-71-4
imibenconazole	86598-92-7
metconazole	125116-23-6
myclobutanil	88671-89-0
penconazole	66246-88-6
propiconazole	60207-90-1
tebuconazole	107534-96-3
tetraconazole	112281-77-3
triadimefon	43121-43-3
triadimenol	55219-65-3
triticonazole	131983-72-7

Under certain conditions, a triazole fungicide frequently is phytotoxic to the very plant species the fungicide is meant to protect from disease. For example triadimefon can be phytotoxic to ornamental plants (The Pesticide Manual, Eleventh Edition, C.D.S. Tomlin, ed., The British Crop Protection Council, Farnham, Surrey, U.K., 1997, p. 1217); metconazole can cause stunting and yellowing of plants (Id., p. 804); hexaconazole can cause damage to McIntosh apples (Id., p. 675); difenoconazole

can cause chlorosis in wheat (Id., p. 390); and bitertanol can cause damage to fruit crops (Id., p. 132).

Controlled release of a pesticide has occasionally been used as a method of controlling phytotoxicity of the pesticide to the beneficial plant species. Patents and published patent applications disclosing various controlled-release formulations include each of the following individual disclosures.

U.S. Patent No. 4,172,119.

10 U.S. Patent No. 4,915,947.

U.S. Patent No. 5,225,278.

U.S. Patent No. 5,277,979.

U.S. Patent No. 5,725,869.

European Patent Publication No. 0 004 758-A2.

15 European Patent Publication No. 0 018 119-A1.

European Patent Publication No. 0 763 510-A1.

PCT Patent Application No. WO 88/08300.

#### SUMMARY OF THE INVENTION

20 Thus, there is a continuing need for controlled-release formulations by which an agricultural chemical can be delivered to a plant over the entire growing season at a concentration or rate which is agronomically effective, while reducing plant phytotoxicity relative to current commercially used practices. There is especially a need for a controlled-release formulation of a fungicide such as a triazole fungicide which can provide effective fungicidal control over a period of time without causing unacceptable phytotoxic damage to an agriculturally beneficial plant to which the formulation is applied.

30

Preferably, such formulations would include an amount of an active ingredient that is close to the minimum amount needed to obtain the desired effect in order to reduce environmental impacts and to reduce costs.

5        Among the many embodiments of the present invention may be noted a controlled-release formulation which comprises a particle in which one or more agricultural active ingredients are dispersed or distributed in a polymeric matrix. Such controlled-release formulations are  
10 safe when applied to seeds or to plants even though they contain levels of active ingredients that would be phytotoxic if applied to the seeds or plants in standard fast-release formulations. The particle of the present invention can release at least one active ingredient at  
15 biocidally beneficial levels over a period during the germination and growth of an agriculturally beneficial plant (e.g., for at least two to twelve weeks or more) and therefore can reduce or eliminate the need for subsequent applications of the agricultural chemical. The rate of  
20 release of agricultural chemicals, and the period over which effective amounts of such chemicals can be released, can be tailored as desired. Such controlled-release compositions thus increase the period during which an agricultural chemical is effective, reduce the initial  
25 toxicity of the chemical to seeds or crop plants, expand the range of compounds that can be used for agricultural applications, and decrease the environmental impact of chemical treatment.

In one embodiment, the present invention presents a  
30 particle comprising a triazole fungicide in a polymer matrix. Preferably, the triazole fungicide comprises a

2025 RELEASE UNDER E.O. 14176

compound selected from the group consisting of bitertanol, bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, hexaconazole, imibenconazole, metconazole, myclobutanil, penconazole, propiconazole, tebuconazole, tetraconazole, triadimefon, triadimenol, and triticonazole. The present invention further embodies a fungicidal composition comprising a particle comprising a triazole fungicide in a polymer matrix, and an agricultural adjuvant.

In another embodiment of the invention, controlled-release compositions for delivering an agricultural chemical to a plant comprise particles having an average diameter of about 0.1 microns to about 200 microns, the particles each comprising a polymer matrix and at least one agricultural chemical distributed throughout the polymer matrix. The particles include about 1 to about 50% by weight of the agricultural chemical and about 50% to about 99% by weight of the polymer matrix.

In a further embodiment, the present invention provides compositions including suspensions of the particles in an aqueous medium, wettable powders, wettable granules, dry granules, and seed coatings, for example. According to at least some embodiments of the invention, the particles adhere to a surface of a seed or plant.

A further embodiment of the present invention comprises compositions which include an amount of the agricultural chemical and which release the agricultural chemical at a rate such that the composition delivers an agriculturally active amount of the agricultural chemical to the plant for a period of at least about two weeks to

about twelve weeks, preferably throughout the growth period of the plant.

In yet another embodiment of the invention, such compositions as described in the present disclosure can be used in a method to reduce the phytotoxicity of the agricultural chemical by at least two-fold (i.e., at least a 50% reduction in phytotoxicity as compared to conventional fast-release formulations of the chemical). For example, in the case of seed coating compositions according to the present invention, the composition can include an amount of the agricultural chemical that would be substantially phytotoxic if applied to the surface of the seed as a fast-release formulation of the agricultural chemical. One embodiment of the present invention provides a method for the treatment or prophylaxis of a fungal disease in a target plant wherein the method comprises contacting a plant cell, a plant tissue, or a seed with a particle wherein the particle comprises a triazole fungicide in a polymer matrix and wherein after the contacting, the health of the target plant is substantially similar to the health of a control plant which is substantially free of the fungal disease and which is free of contact with the triazole fungicide.

Another embodiment of the present invention provides a method for the treatment or prophylaxis of a fungal disease in a target plant wherein the method comprises contacting a plant cell, a plant tissue, or a seed with a particle wherein the particle comprises a triazole fungicide in a polymer matrix and wherein after the contacting, the health of the target plant is intermediate between the health of a first control plant which is substantially free of the

5 fungal disease and which is free of contact with the triazole fungicide, and the health of a second control plant which is substantially free of the fungal disease and which is contacted with the triazole fungicide in the absence of the polymer matrix. Commercially acceptable levels of disease control (e.g., fungal control) frequently results from plants in which less than 100% of the disease agent (e.g. a fungus) has been eradicated. For example, in some circumstances and markets, a treatment providing 60-10 80% fungal disease control is considered commercially acceptable.

15 In a further embodiment of the invention, the agricultural chemical comprises a biocide (e.g., a triazole fungicide such as bitertanol, bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, hexaconazole, imibenconazole, metconazole, myclobutanil, penconazole, propiconazole, tebuconazole, tetraconazole, triadimefon, triadimenol, or triticonazole), a plant growth regulator, a20 chemical hybridizing agent, a plant nutrient, or combinations thereof.

25 In one embodiment, the polymer used in the compositions of the present invention is selected from the group consisting of poly(methylmethacrylate), poly(lactic acid), poly(lactic acid-glycolic acid) copolymers, cellulose acetate butyrate, poly(styrene), hydroxybutyric acid-hydroxyvaleric acid copolymers, styrene maleic anhydride copolymers, poly(methylvinyl ether-maleic acid), poly(caprolactone), poly(n-amylmethacrylate), wood rosin,30 polyanhydrides, polyorthoesters, poly(cyanoacrylates), poly(dioxanone), ethyl cellulose, ethyl vinyl acetate

polymers, poly(ethylene glycol), poly(vinylpyrrolidone),  
acetylated mono-, di-, and triglycerides,  
poly(phosphazene), chlorinated natural rubber, vinyl  
polymers, polyvinyl chloride, hydroxyalkylcelluloses,  
5 polybutadiene, polyurethane, vinylidene chloride polymers,  
styrene-butadiene copolymers, styrene-acrylic copolymers,  
alkylvinylether polymers, cellulose acetate phthalates,  
ethyl vinyl phthalates, cellulose triacetate,  
polyanhydrides, polyglutamates, polyhydroxy butyrates,  
10 polyvinyl acetate, vinyl acetate-ethylene copolymers, vinyl  
acetate-vinylpyrrolidone copolymers, acrylic polymers,  
alkyl acrylate polymers, aryl acrylate polymers, aryl  
methacrylate polymers, poly(caprolactams), epoxy resins,  
polyamine epoxy resins, polyamides, polyvinyl alcohol  
15 polymers, polyalkyd resins, phenolic resins, abietic acid  
resins, silicones, polyesters, and copolymers and  
combinations thereof.

The present invention further embodies compositions which include a dispersing agent, such as methyl cellulose, poly(vinyl alcohol), lecithin, and combinations thereof.

In another embodiment of the invention, seeds are provided that comprise such compositions, e.g., as seed coatings.

A further embodiment of the invention provides a method for delivering an agricultural chemical to a plant wherein the method comprises providing to the plant a composition as discussed above, for example, by application of the composition to soil, application of the composition to foliage of the plant, and coating a seed prior to germination of the seed to produce the plant. When applied to soil or foliage the composition can be applied, for



example, in an amount such that about 1 g to about 10 kg of the agricultural chemical is applied per hectare. When applied as a seed coating, the composition can be applied in an amount such that about 1 gram to about 500 grams of the agricultural chemical is applied to 100 kg of seed.

In a further embodiment of the invention, methods are provided for producing the compositions described above. Such methods include the steps of: (a) dissolving at least one agricultural chemical (for example, a triazole fungicide) and a polymer in a to form a hydrophobic solution; (b) mixing the hydrophobic solution and an aqueous medium at a shear rate and for a time period sufficient to produce an emulsion having droplets of the hydrophobic solution dispersed in the aqueous medium; and (c) evaporating the organic solvent from the emulsion to produce a plurality of particles having an average diameter of about 0.2 micron to about 200 microns and comprising said at least one agricultural chemical distributed throughout a polymer matrix. According to some embodiments of the invention, such methods include one or more of the further steps of: dissolving a dispersing agent in an aqueous solution to produce the hydrophilic solution; and suspending the particles in an aqueous medium.

A preferred embodiment of the present invention provides a method of producing a particle wherein the particle comprises a triazole fungicide in a polymer matrix, and the method comprises providing a hydrophobic solution comprising a triazole fungicide, a polymer, and a solvent; mixing the hydrophobic solution and an aqueous medium to produce a dispersion of droplets of the hydrophobic solution in the aqueous medium; and evaporating

the solvent from the dispersion to produce a particle comprising a triazole fungicide in a polymer matrix.

A further embodiment of the present invention provides a method of producing a particle wherein the particle comprises a triazole fungicide in a polymer matrix, the method comprising the steps of providing a hydrophobic solution comprising a triazole fungicide, a polymer, and a solvent; mixing the hydrophobic solution and an aqueous medium to produce a dispersion of droplets of the hydrophobic solution in the aqueous medium; and evaporating the solvent from the dispersion to produce a particle comprising a triazole fungicide in a polymer matrix.

The present invention also embodies a method for the treatment or prophylaxis of a fungal disease in a target plant wherein the method comprises contacting a plant cell, 15 a plant tissue, or a seed with a particle wherein the particle comprises a triazole fungicide in a polymer matrix.

Other aspects of the present invention will become  
20 apparent to those skilled in the art upon studying this  
disclosure and the accompanying claims.

### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows the effect of matrix particle formulations of Example 7 and Alto 005LS when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat at 11 days after planting (DAP) as a percent of the height of untreated controls.

FIG. 2 shows the effect of matrix particle formulations of Example 8 and Alto 005LS when used as seed

treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat at 10 DAP as a percent of the height of untreated controls.

FIG. 3 shows the effect of matrix particle  
5 formulations of Example 9 and Alto 005LS when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat at 10 DAP as a percent of the height of untreated controls.

FIG. 4 shows the effect of matrix particle  
10 formulations of Example 10 and Alto 005LS when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat at 11 DAP as a percent of the height of untreated controls.

FIGS. 5 and 6 show the effect of a matrix particle  
15 formulation of Example 11, Formulation 29, and Alto 005LS when used as a seed treatment on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat at 10 DAP (FIG. 5) or 9 DAP (FIG. 6) as a percent of the height of untreated controls.

20 FIG. 7 shows the effect of matrix particle formulations of Example 12, Formulation 29, Formulation 31, and Alto 005LS, when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat as a percent of the  
25 height of untreated controls at 9 DAP.

FIG. 8 shows the effect of matrix particle  
formulations of Example 12, Formulation 31, Formulation 32, and Alto 005LS, when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed  
30 as the height of germinating wheat as a percent of the height of untreated controls at 10 DAP.

FIG. 9 shows the effect of matrix particle formulations of Example 13, Formulation 33 and Formulation 34, and Alto 005LS, when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat as a percent of the height of untreated controls at 10 DAP.

FIG. 10 shows the effect of a matrix particle formulation of Example 13, Formulation 35, and Alto 005LS, when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat as a percent of the height of untreated controls at 10 DAP.

FIG. 11 shows the effect of matrix particle formulations of Example 14 and Alto 005LS when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat as a percent of the height of untreated controls at 10 DAP.

FIG. 12 shows the effect of matrix particle formulations of Example 15 and Alto 005LS when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat as a percent of the height of untreated controls at 10 DAP.

FIG. 13 shows the effect of matrix particle formulations of Example 16 and Alto 005LS when used as seed treatments on wheat at various rates (g cyproconazole per 100 kg seed), expressed as the height of germinating wheat as a percent of the height of untreated controls at 10 DAP.

FIG. 14 shows the effect of matrix particle  
30 formulations of Examples 17 and 18, Formulation 43 and  
Formulation 44, respectively, and Raxil when used as seed

treatments on wheat at various rates (g tebuconazole per 100 kg seed), expressed as the height of germinating wheat as a percent of the height of untreated controls at 11 DAP.

FIG. 15 shows the effect of matrix particle  
5 formulations of Examples 19 and 20, Formulation 45 and Formulation 46, respectively, and Opus when used as seed treatments on wheat at various rates (g epoxiconazole per 100 kg seed), expressed as the height of germinating wheat as a percent of the height of untreated controls at 11 DAP.

10 FIG. 16 shows the effect of matrix particle formulations of Example 21 at an application rate of 16 g cyproconazole per 100 kg seed and Alto 005LS when used as seed treatments on wheat, expressed as the height of germinating wheat as a percent of the height of untreated  
15 controls at 8 DAP.

FIG. 17 shows control of brown rust of wheat (second leaf) by seed coatings comprising matrix particle Formulation 47, Formulation 15, Formulation 77 (each at 32 g cyproconazole per 100 kg seed), and Alto 005LS (1 g  
20 cyproconazole per 100 kg seed). Plants were inoculated 20 DAP. Disease severity in untreated controls was 61.3%.

#### DETAILED DESCRIPTION OF THE INVENTION

The following detailed description is provided to aid those skilled in the art in practicing the present  
25 invention. Even so, this detailed description should not be construed to unduly limit the present invention as modifications and variations in the embodiments discussed herein can be made by those of ordinary skill in the art without departing from the spirit or scope of the present  
30 inventive discovery.

The contents of each of the references cited herein, including the contents of the references cited within these primary references, are herein incorporated by reference in their entirety.

5

**a. Definitions**

The following definitions are provided in order to aid the reader in understanding the detailed description of the present invention:

10 "Agricultural chemical" or "active ingredient" means a chemical which is useful in the control of a disease or a pest (including without limitation a weed, an insect, a parasite, and a fungus) in agricultural settings.

The abbreviation "a.i." means active ingredient.

15 "Phytotoxic" means injurious to vegetation.

"Agronomic plant" means a plant useful in agriculture and which is sought to be protected from disease or pests.

"Agriculturally beneficial" means useful or productive in agriculture.

20 "Agricultural adjuvant" or "inert ingredient" means a material used in an agricultural formulation or composition to aid in the operation or to improve the effectiveness of an agricultural chemical. The term includes such materials as a wetting agent, a spreader, an emulsifier, a dispersing agent, a foaming adjuvant, a foam suppressant, an antifoam, 25 a penetrant, a corrective, a surfactant, a solvent, a solubilizer, a buffering agent, and a sticker.

The term "combination" is intended to embrace application of each agent in a sequential manner in a 30 regimen that will provide beneficial effects of the agricultural chemical combination, and is intended as well

6640990-11092260

to embrace compositions or co-administration of these agents in which the presence or application of these agents occurs in a substantially simultaneous manner, such as in a single spray mixture or treatment having a fixed ratio of these active agents.

**b. Compositions and Methods**

The matrix particle formulations of this invention are useful in agriculture for a number of purposes, including, for example, the control of seed-borne and soil-borne pathogens and pests, as well as pests affecting above-ground portions of plants (for example, stems, foliage, flowers, fruits), and underground portions (for example, roots, rhizomes, tubers) for the delivery of nutrients, chemical hybridizing agents and plant growth regulators, and the like. It will also be appreciated that such formulations have a number of non-agricultural uses, such as in the delivery of pharmaceuticals to humans or to animals for therapeutic or prophylactic purposes; for the controlled release of chemicals in water treatment or conditioning, aquaculture, etc.

Controlled-release formulations according to the present invention substantially reduce the phytotoxicity of an agricultural chemical to a seed or a plant compared to a standard fast-release formulation of the chemical (i.e., one having a release rate that is substantially similar to that of the unformulated chemical). That is, such controlled-release formulations reduce the toxicity of, and correspondingly increase the "safety" of (or "safen"), the agricultural chemical. Therefore, for a given level of phytotoxicity, more of the chemical can be applied to a

seed or a plant in the form of a controlled-release formulation according to the present invention than in a standard fast-release formulation. Preferably, a controlled-release formulation according to the present invention safens a particular chemical by at least two-fold (i.e., at least a 50% reduction in phytotoxicity as compared to conventional fast-release formulations of the chemical), more preferably by at least five-fold (i.e., at least a 80% reduction in phytotoxicity as compared to conventional fast-release formulations of the chemical), yet more preferably by at least ten-fold (i.e., at least a 90% reduction in phytotoxicity as compared to conventional fast-release formulations of the chemical), and most preferably by at least twenty-fold (i.e., at least a 95% reduction in phytotoxicity as compared to conventional fast-release formulations of the chemical). In fact, we have applied greater than one hundred times the amount of standard formulations of certain phytotoxic chemicals with only minimal injury to plants. As shown in the Examples below, the safening of various agricultural chemicals such as triazole fungicides permits their use as seed treatments at levels that would otherwise prevent germination or stunt the growth of plants that germinate from the seeds, making them more effective against various pathogens and pests.

25

**Matrix particle.** The term "matrix" is defined as a surrounding material in which another material is entrapped, embedded, dissolved, dispersed or otherwise distributed. Particles of the present invention comprise a matrix that includes one or more polymers in which one or



more active ingredients are entrapped, embedded, dissolved, dispersed, or otherwise distributed. The particles may also include one or more inert ingredients or additives, such as dispersants. The particles of the present  
5 invention differ from "microcapsules," in which a polymeric shell surrounds a liquid or solid core that contains an active ingredient. The core of the particle may be divided into a number of separate domains or multiple cores. In at least some embodiments of the particles of the present  
10 invention, the final product appears in freeze-fracture electron micrographs as solid, generally spherical particles that appear solid throughout, indicating that the active ingredient(s) is distributed or dispersed within the matrix material. The distribution may be at a molecular  
15 level or the distribution may be as finely divided pockets comprising a plurality of molecules of the active ingredient. The distribution may be substantially uniform throughout the matrix material or the distribution may exhibit a concentration gradient through a cross-section of  
20 the matrix material. Therefore it is possible in at least some embodiments that an active ingredient may be macromolecularly distributed in the matrix, i.e., that a plurality of particles of the active ingredient are dispersed in the matrix.

25 The agriculturally active ingredient can comprise about 1.0% to about 50% by weight, preferably about 15% to about 50% by weight of the particle of the present invention. The particle can comprise from about 50 to about 99% by weight of matrix material. It is preferred  
30 that the particle comprise from about 50% to about 90% by weight of the matrix material. It is particularly

2025 RELEASE UNDER E.O. 14176

economical if the particle comprises a high proportion of the active ingredient. If the proportion of matrix material to entrapped active ingredient is too high, the rate of release of the entrapped material may decrease, thereby causing a decrease in the biological efficacy of the treatment, and causing an increase in the cost of a biologically effective amount of the final product. If the proportion of the matrix component to the entrapped material component is too small, the rate of release may be unacceptably high, leading to phytotoxicity and reducing the period of effectiveness of the active ingredient. As the concentration of the active ingredient increases in the particle, the release rate will also generally increase.

The average matrix component concentration, as a percent of the total weight of the matrix particle (combined weight of matrix, active ingredient and any other ingredients associated with the polymer matrix), can be estimated from the amount of ingredients in the composition used for preparing the particle.

The particle of the present invention preferably has an average particle size in the range of about 0.2 microns to about 200 microns in diameter. Release rate of the active ingredient is generally inversely proportional to the average particle size. Frequently plant phytotoxicity of the treatment comprising the particle of the present invention is inversely proportional to the average particle size. Smaller average particle sizes generally have a higher release rate and area coverage of active ingredient, together with a higher activity and phytotoxicity of the active ingredient. Conversely, larger average particle sizes are associated with low area coverage and reduced

phytotoxicity, but also lower activity and phytotoxicity. In addition, the small size of the particle of the present invention will permit the particle to be taken up by a plant together with soil water and to be transported  
5 throughout the plant, effecting systemic delivery of active ingredient. The average particle size is preferably about 1 micron to about 50 microns in diameter, more preferably about 3 to about 50 microns. The size of the matrix particles is controlled during the process of entrapment by  
10 employing a mixing, stirring, or agitating means (for example, a blender, a rotostator, a shaker, a vibrator, a homogenizer, a mill, a microdropping syringe, or a sonicator at a suitable rate of speed to form droplets of the ingredients to be entrapped.

15 The particle size distribution of a batch of matrix particles of the present invention can be monomodal, bimodal, or polymodal. The different modalities can offer different advantages depending upon the desired application. For example, a monomodal particle size  
20 distribution may provide a relatively uniform release rate of the active ingredient. In contrast, a bimodal or a polymodal particle size distribution may provide more than one release rate of the active ingredient, thereby affording an active ingredient release rate profile  
25 tailored to the specific agricultural situation.

The particle size of the matrix particle of this invention is measured by using a microscope with a calibrated reticle and visually estimating the average particle size. Alternatively, the size can be determined  
30 by electronic means, for example by using a Coulter LS Counter or by laser light scattering. Microscopic

determination generally is within 5 microns of the size measured by the Coulter Counter. From the distribution of particle sizes,  $d_{16}$ ,  $d_{50}$  and  $d_{84}$  values are determined and plotted in a log probability plot. The  $d_{16}$  value represents  
5 the size (diameter in microns) at which 16 weight percent of the capsules in the sample are equal to or larger than  $d_{16}$ ,  $d_{50}$  represents the size at which 50 weight percent of the capsules are equal to or greater in diameter than  $d_{50}$ , and  $d_{84}$  represents the size at which 84 weight percent of  
10 the particles are equal to or greater in diameter than  $d_{84}$ .

The particle of the present invention preferably adheres to the surface of a seed or a plant. Without being limited by theory, it is thought that the particle becomes trapped in microhairs or in crevices on the seed or plant  
15 surface. Alternatively, the particle may adhere to a surface moiety of the plant, such as to the cuticle. Adhesion of the particle to the seed or the plant can be enhanced or achieved by the use of conventional "sticking agents" (i.e., "stickers" or "tackifiers") or other  
20 compounds that have been used for applying various coatings to seeds.

Particles can affect the mobility of an active ingredient in soil, since the binding or retention of the particle to soil can be substantially different than the  
25 binding of the active ingredient itself. As a result, depending on the matrix material selected, the composition according to the present invention can increase the effectiveness of an agricultural chemical that would be rendered less effective due to tight binding of the  
30 agricultural chemical to soil.

Also encompassed by the present invention is a particle comprising an agricultural chemical (such as a triazole fungicide) in a polymer matrix wherein the particle further comprises an encapsulation shell or coating on the surface of the particle. Such shell or coating can be applied to the particle by conventional methods and can provide further control of release of active ingredients, add additional active or other ingredients, or confer desirable properties to the resulting product.

**Polymer.** The term "polymer" or "polymeric material" as used in this invention is taken to mean either a single polymer or a combination of different polymers or a copolymer. The particle comprises from about 50% to about 99% by weight of the polymeric material, preferably from about 50% to about 90% by weight.

A matrix material is selected so that the rate of release of the active ingredient provides an "agriculturally effective amount" of the active ingredient, i.e., an amount of the active ingredient that is effective to achieve a desired level crop protection or other desired agricultural activity characteristically associated with the agricultural chemical. Thus, for a biocide, an agriculturally effective amount is an amount that is sufficient to provide commercially acceptable control of a pathogen or pest; for a plant growth regulator, an amount that is sufficient to substantially alter the growth or development of the plant in a manner characteristic of the plant growth regulator; for a nutrient, an amount that is sufficient to provide at least the minimum amount of the nutrient required for normal plant growth and development.

Preferably, the active ingredient is released at a rate that does not cause substantial phytotoxicity, i.e., does not reduce the growth or vigor of the plant to commercially unacceptable levels or produce other types of unacceptable damage to the plant. Preferably, the active ingredient is released at beneficial levels throughout the period of germination, emergence, later developmental stages of the crop or plant, or throughout the entire growth period of the plant. The active ingredient may be released by diffusion from the matrix or by the degradation or dissolution of the matrix in the plant, soil or foliar environment. In addition, the polymer and breakdown products thereof, if any, should not substantially interfere with the effectiveness of the active ingredient (or other components, such as the dispersing agent) or be substantially phytotoxic to the seed, seedling or plant.

Examples of suitable polymers for the practice of this invention include but are not limited to the following non-exhaustive list of polymers (and copolymers and mixtures thereof):

- poly(methylmethacrylate)
- poly(lactic acid) (Chronopols 50, 95, and 100)
- and copolymers such
- as poly(lactic acid-glycolic acid)
- copolymers (Lactel BP-400) and combinations
- with polystyrene, for example
- cellulose acetate butyrate
- poly(styrene)
- hydroxybutyric acid-hydroxyvaleric acid
- copolymers
- (Biopol D400G)

styrene maleic anhydride copolymers  
(SMA 1440 A Resin, Sartomer Co.)  
poly(methylvinyl ether-maleic acid)  
poly(caprolactone)  
poly(n-amylmethacrylate)  
wood rosin  
polyanhydrides, e.g., poly(sebacic anhydride),  
poly(valeric anhydride), poly(trimethylene  
carbonate), etc., and  
copolymers such as  
poly(carboxyphenoxypropane-sebacic acid),  
poly(fumaric acid-sebacic acid), etc.  
polyorthoesters  
poly(cyanoacrylates)  
poly(dioxanone)  
ethyl cellulose  
ethyl vinyl acetate polymers and copolymers  
poly(ethylene glycol)  
poly(vinylpyrrolidone)  
acetylated mono-, di-, and triglycerides  
poly(phosphazene)  
chlorinated natural rubber  
vinyl polymers and copolymers  
polyvinyl chloride  
hydroxyalkylcelluloses  
polybutadiene  
polyurethane  
vinylidene chloride polymers and copolymers  
styrene-butadiene copolymers  
styrene-acrylic copolymers  
vinyl acetate polymers and copolymers (e.g.,

061050" 47092260

vinyl acetate-ethylene copolymers  
(Vinumuls) and vinyl acetate-  
vinylpyrrolidone copolymers  
alkylvinylether polymers and copolymers  
cellulose acetate phthalates  
ethyl vinyl phthalates  
cellulose triacetate  
polyanhydrides  
polyglutamates  
polyhydroxy butyrates  
acrylic polymers (Rhoplexes)  
alkyl acrylate polymers and copolymers  
aryl acrylate polymers and copolymers  
aryl methacrylate polymers and copolymers  
poly(caprolactams) (i.e., the nitrogen-  
containing counterparts to caprolactones)  
epoxy/polyamine epoxy/polyamides  
polyvinyl alcohol polymers and copolymers  
silicones  
polyesters (for oil-based approaches,  
including alkyds)  
phenolics (polymers and copolymers with drying  
oils)

Preferred polymers include:

poly(methylmethacrylate)  
poly(lactic acid) (Chronopols 50, 95, or 100)  
and combinations with polystyrene  
poly(lactic acid-glycolic acid) copolymers  
(Lactel BP-400)  
cellulose acetate butyrate



poly(styrene)

Poly(methylmethacrylate or poly(styrene maleic anhydride copolymer) (or blends comprising one or both of these polymers) are currently preferred for use with triazole fungicides such as tebuconazole, cyproconazole, and  
5 epoxiconazole, for example.

It is also contemplated that certain resins such as polyalkyd resins, phenolic resins, abietic acid and epoxy resins will be suitable for the practice of this invention. Also encompassed by the present invention are filled  
10 polymer and co-polymer systems, i.e., using calcium carbonate, silica, clay, and the like.

**Active Ingredient.** The particle of the present invention can include an active ingredient entrapped in a polymeric matrix or a plurality of active ingredients  
15 having similar or different activities (e.g., a fungicide and an insecticide). The active ingredient can be, for example,, any of various conventional biocides, including a fungicide (e.g., a triazole, an imidazole, a methoxyacrylate, a fungicide in the morpholine series such  
20 as fenpropimorph), a herbicide (e.g., glyphosate, phosphinothricin, triallate, alachlor), a insecticide (e.g., an organophosphorus compound, imidacloprid, a pyrethroid), a nematocide (e.g., Tribute), an acaricide, a molluscicide, a nematocide, a rodenticide, a bactericide,  
25 and a termiticide; a chemical hybridizing agent (e.g., clofenset potassium); a herbicide safener; a chemical inducer or elicitor (e.g., a protein activator), a plant growth regulator (e.g., an auxin, a cytokinin, or a gibberellin), an elicitor, or a nutrient such as a

661030-11032E60

fertilizer, or a minerals). In addition to an active ingredient, the particle can also include one or more inert ingredients such as a solvent, a dispersant, an adjuvant, or a plasticizer, and can be formulated for example as a liquid, a dispersion, a water soluble granule, a wettable powder, a water dispersible granule, a suspension concentrate, a liquid flowable, an dry flowable, a suspension, a granule, or a seed coating. Triazole fungicides suitable for the practice of this invention are exemplified by bitertanol, bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, hexaconazole, imibenconazole, metconazole, myclobutanil, penconazole, propiconazole, tebuconazole, tetraconazole, triadimefon, triadimenol, and triticonazole. Preferably the triazole fungicide is selected from the group consisting of cyproconazole, epoxiconazole, tebuconazole, triadimefon, and triadimenol. More preferably the triazole fungicide is cyproconazole. A discussion of the properties for some of these fungicides can be found in U.S. patent No. 4,664,696, EPA 196038, and U.S. patent 4,723,984.

Some representative fungicides, herbicides, insecticides, and growth regulators that are useful in the present invention are listed below:

Fungicides	
benomyl	fludioxonil
benzothiadiazoles	flutolanil
captan	fosetyl-Al
chlorothalonil	kresoxim-Methyl
cyproconazole	mancozeb
cyprodinil	metalaxyl
epoxiconazole	prochloraz
fenarimol	triticonazole
fenpropimorph	tebuconazole
bitertanol	vinclozolin
bromuconazole	difenoconazole
epoxiconazole	fenbuconazole
fluquinconazole	flusilazole
flutriafol	hexaconazole
imibenconazole	metconazole
myclobutanil	penconazole
propiconazole	tetraconazole
triadimefon	triadimenol

Herbicides
acetochlor
acifluorfen
acrolein
alachlor
ametryn
amitrole
anilofos
asulam
atrazine
benazolin
benefin
benfluralin
bensulfuron
bensulfuron-methyl
bensulfide
bentazone
bifenox
bromacil
bromoxynil
butachlor
butralin

butylate
carfentrazone
carfentrazone-ethyl
chloramben
chlordiazon
chlorflurenol
chlorimuron
chlorotoluron
chloroxuron
chlorpropham
chlorsulfuron
cinmethylin
clethodim
clomazone
clopyralid
cyanazine
cycloate
cinmethylin
2,4- dichlorophenoxyacetic acid
2,4- dichlorophenoxyacetic acid methyl ester
dalpon
dazomet
2,4-DB
DCPA
desmedipham
diallate
dicamba
diclobenil
dichlormid
dichlorprop
diclofop
diethatyl
dietholate
difenzoquat
dinoseb
diphenamid
dipropetryn

667090"TF092260

diquat
diuron
EPTC
ethalfluralin
ethofumesate
fenac
fenoxaprop
fenoxaprop-ethyl
fenuron TCA
fluazifop
fluazifop-P
fluchloralin
flumetsulam
fluometuron
fluroglycofen
fluroglycofen-ethyl
flurazole
flurenol-butyl
fluridone
fomesafen
fosamine
glufosinate
glyphosate
haloxyfop
halosulfuron
halosulfuron-methyl
hexazinone
imazameth
imazamethazenz
imazamethabenz-methyl
imazapyr
imazaquin
imazethapyr
ioxynil
isopropalin
isoproturon
isoxaben
lactofen
linuron
MAA

667090-1709260

MCPA
MCPB
mecoprop
mefenacet
mefluidide
metham
methazole
metolachlor
metribuzin
metsulfuron
MH
molinate
monolinuron
MSMA
naproanilide
napropamide
naptalam
neburon
nicosulfuron
norea
norflurazon
orbencarb
oryzalin
oxadiazon
oxyfluorfen
paraquat
pebulate
pelargonic acid
pendimethalin
phenmedipham
picloram
primisulfuron
prodiamine
prometon
prometryn
pronamide
propachlor
propanil
propazine
propham

00226014-060409

pyrazon
pyrazosulfuron
pyrazosulfuron-ethyl
pyridate
quizalofop
quizalofop-ethyl
rimsulfuron
sethoxydim
siduron
simazine
simetryn
sulfometuron
tebuthiuron
terbacil
terbuthylazine
terbumeton
terbutryn
thifensulfuron
thiobencarb
triallate
triasulfuron
triclopyr
trifluralin
vernolate

Insecticides and Nematicides	
aldicarb	fenvalerate
azinphos-methyl	imidachloprid
carbaryl	lindane
carbofuran	malathion
chlorpyrifos	methyl Parathion
cyfluthrin	monocrotophos
diazinon	oftanol
dicofol	oxamyl
disulfoton	parathion
endosulfan	propoxur
fenamiphos	pyrethrins

<b>Growth Regulators</b>
--------------------------

0925014-060409

6-benzyladenine	endothall
alpha-naphthylactic acid	ethepon
ancymidol	gibberellic acid
chlorpropham	maleic Hydrazine
daminozide	paclobutrazol

<b>Chemical Hybridizing Agents</b>
------------------------------------

clofenset (K <sup>+</sup> salt)
---------------------------------

Accordingly, in one embodiment the present invention comprises a particle comprising a triazole fungicide in a polymer matrix. For example, the triazole fungicide can comprise a compound selected from the group consisting of bitertanol, bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, hexaconazole, imibenconazole, metconazole, myclobutanil, penconazole, propiconazole, tebuconazole, tetraconazole, triadimefon, triadimenol, and triticonazole. Preferably the triazole fungicide comprises a compound selected from the group consisting of cyproconazole, epoxiconazole, tebuconazole, triadimefon, and triadimenol.

The polymer matrix can comprise a polymer selected from the group consisting of poly(methylmethacrylate), poly(lactic acid), a poly(lactic acid-glycolic acid) copolymer, cellulose acetate butyrate, a poly(styrene), hydroxybutyric acid-hydroxyvaleric acid copolymer, a styrene maleic anhydride copolymer, poly(methylvinyl ether-maleic acid), poly(caprolactone), poly(n-amylmethacrylate), wood rosin, a polyanhydride, a polyorthoester, a poly(cyanoacrylate), poly(dioxanone), ethyl cellulose, a ethyl vinyl acetate polymer, poly(ethylene glycol), poly(vinylpyrrolidone), an acetylated monoglyceride, an acetylated diglyceride, an acetylated triglyceride, poly(phosphazene), chlorinated



natural rubber, a vinyl polymer, polyvinyl chloride, a hydroxyalkylcellulose, polybutadiene, polyurethane, a vinylidene chloride polymer, a styrene-butadiene copolymer, a styrene-acrylic copolymer, an alkylvinylether polymer, a cellulose acetate phthalate, an ethyl vinyl phthalate, cellulose triacetate, a polyanhydride, a polyglutamate, a polyhydroxy butyrate, polyvinyl acetate, a vinyl acetate-ethylene copolymer, a vinyl acetate-vinylpyrrolidone copolymer, an acrylic polymer, an alkyl acrylate polymer, an aryl acrylate polymer, an aryl methacrylate polymer, a poly(caprolactam), an epoxy resin, a polyamine epoxy resin, a polyamide, a polyvinyl alcohol polymer, a polyalkyd resin, a phenolic resin, an abietic acid resin, a silicone, a polyalkylene oxide, and a polyester.

15           The particle of the present invention can further  
comprise other ingredients including inert ingredients.  
For example, the inventive particle can comprise a  
plasticizer.

The present invention can comprise a particle having a variety of diameters or average diameters. For example, the mean diameter of the particle can be in the range of from about 0.1 microns to about 200 microns, preferably from about 0.2 microns to about 100 microns, and more preferably from about 0.5 microns to about 50 microns.

25

Release of Active Ingredient from the Particle. The particle according to the present invention can release an agricultural chemical in a controlled fashion by diffusion (e.g., in the case of a particle having a polymer matrix comprising poly(methylmethacrylate or poly(styrene maleic

anhydride copolymer) or by disintegration or dissolution of the matrix (e.g., in the case of a particle having a polymer matrix comprising polylactic acid polymers), depending on the matrix polymer employed. Release rates  
5 also vary with the size of particles (i.e., release rates vary as a function of the surface area/volume ratio of the particle). The matrix material can be selected to have properties conducive to the appropriate release and action of the agriculturally active ingredient in space and time.  
10 A particle can also be prepared such that the active ingredient varies in concentration from the outer surface of the matrix particle to its core, providing "programmed" rates and levels of active release over the duration of the seed germination and subsequent growth periods.

15 The rate of release of an active ingredient from a particle according to the present invention depends on the polymer, size of the particle, the loading of the active ingredient, and the dispersing agent used, if any. The manner in which an active ingredient can be released from a  
20 particle depends on whether the loaded active ingredient is suspended or dissolved in the matrix. The steps involved when the active ingredient is dissolved in the matrix material include: diffusion of the active ingredient to the surface of the matrix; partition of the active  
25 ingredient between the matrix and the environment or elution medium (e.g., soil water, seed coat, or foliar surface); and transport away from the particle surface. In addition, if the active ingredient is dispersed (for example, as multimolecular pockets of active ingredient in  
30 the particle), the active ingredient may have to dissolve into the matrix material before diffusion to the surface.

1564050-4T032200

Another mode of release of the active ingredient can be by biodegradation or erosion of the matrix material, the rate of which can be influenced by the hydrophobicity or hydrophilicity of the polymer, the morphology of the particle, and the chemical nature of the polymer comprising the matrix for example. In addition, the active ingredient can be released by swelling of the polymer matrix after imbibition of a liquid such as water. In diffusion-controlled systems the matrix may be unaffected by swelling, but in swelling-controlled systems the polymer matrix may undergo a transition from a glassy state to a gel state upon interaction with the penetrating solvent. In such cases, release rate can be a function of the glass-to-gel transition process.

Another factor affecting release rate is osmotic pressure, which can be created inside the particle if the active ingredient or polymer has an affinity for the environment external to the particle. The active ingredient is released when the osmotic pressure exceeds the maximum force that the matrix of the particle can tolerate.

Mathematical models for these release mechanisms are described in the following individual references:

U. Pothakamury and G. Barbosa-Canovas, *Trends in Food Science & Technology* 6:397-406, 1995.

R. Langer and N. Peppas, *JMS-Rev. Macromol. Chem. Phys.* C(23):61-126, 1983.

**Formulations Including the Particle.** The particle according to the invention can be used according to any conventional formulation, including but not limited to: a

5

10

15

20

25

30

Formulations according to the present invention can be applied by any conventional method, including but not limited to: (1) direct injection into the soil around seeds or in the root zone of developing plants, for  
5 example, at a point 2 cm deep and within a 3 cm radius of the plant crown; (2) application as a soil drench; (3) application as a foliar spray; and (4) application as a seed treatment.

Particles according to the present invention can be  
10 applied to seeds by any standard seed treatment methodology, including but not limited to mixing in a container (e.g., a bottle or bag), mechanical application, tumbling, spraying, and immersion. Any conventional active or inert material can be used for coating seeds with  
15 particles according to the present invention, such as conventional film-coating materials including but not limited to water-based film coating materials such as Sepiret (Seppic, Inc., Fairfield, NJ) and Opacoat (Berwind Pharm. Services, Westpoint, PA).

20 The formulated product, when used as a suspension in an aqueous carrier, preferably comprises a dispersing agent to permit a relatively uniform or homogeneous mixture to form. The dispersing agent preferably also provides a degree of "tackiness" or adhesion to the particle  
25 formulation in order for the formulation to adhere to treated seeds or other foliar surfaces. Suitable dispersing agents include but are not limited to aqueous 0.25-1.0% poly(vinyl alcohol), such as Elvanol 51-05 (DuPont) and Methocel A15LV.

30 One embodiment of the present invention provides a fungicidal composition comprising a particle comprising a

DOWNSIDE "TFOSEED"

1 triazole fungicide in a polymer matrix, and an agricultural  
adjuvant. The composition can take a variety of forms,  
including a liquid suspension, a wettable powder, a  
granule, a water-dispersible granule, a suspension  
5 concentrate, or the like. Preferably, the fungicidal  
composition comprises a dispersant. The fungicidal  
composition also preferably comprises an adjuvant. The  
fungicidal composition can also comprise a diluent. The  
diluent can be either a solid or a liquid diluent. Solid  
10 diluents can include, for example, silica, alumina,  
cellulose, methylcellulose, clay, or a polymer. Liquid  
diluents can include, for example, water, an organic  
solvent, or an inorganic solvent.

15 Methods of producing matrix particles. The matrix  
particles of the present invention can be produced by any  
process that results in a polymer matrix having active  
ingredients substantially uniformly distributed therein,  
including but not limited to solvent evaporation, solvent  
20 partition, hot melt microencapsulation, coacervation,  
emulsion polymerization, interfacial polycondensation, and  
spray drying.

A preferred process for entrapping the agriculturally  
active ingredient in accordance with the present invention  
25 includes the following steps:

(A) Preparation of a hydrophobic solution ("oil  
phase") including an active ingredient and a polymer in an  
organic solvent;

(B) Preparation of a hydrophilic solution ("aqueous  
30 phase") by dissolving a dispersing agent in water (or an  
aqueous or alcoholic solution);

(C) Forming an emulsion by combining the hydrophobic solution with the hydrophilic solution with stirring, homogenization, or sonication;

(D) Stirring the emulsion formed in (C) until all of  
5 the organic solvent has evaporated. The organic solvent  
can alternatively or additionally be removed at reduced  
pressure using a rotary evaporator; and

(E) Optionally isolating the matrix particles by allowing the evaporated emulsion formed in (D) to settle, decanting the supernatant liquid from the matrix particles, then washing, filtering, and drying the particles in air. The particles can be resuspended in an aqueous carrier system comprising water and, for example, a dispersing agent, dye or colorant, or other inert ingredient. The particles can alternatively be used without isolation.

Specifically, the matrix particle preparation process can be carried out by dissolving the agriculturally active ingredient and the polymer in an amount of organic solvent sufficient to form the hydrophobic solution. This dissolution is performed at room temperature or at temperatures not greater than 50°C with mechanical stirring. For microencapsulating active ingredients according to this general process, it is preferred that the active ingredient be preferentially soluble in the hydrophobic phase rather than in the hydrophilic phase, and preferably substantially insoluble in the aqueous phase (by substantially insoluble is meant a solubility of less than 1% by weight in water at 25°C). A dispersing agent can then be dissolved in a quantity of deionized water sufficient to form the hydrophilic solution. This dissolution is performed at room temperature with mechanical stirring. The hydrophobic

solution is then poured into the hydrophilic solution, while stirring, homogenizing, or sonicating the hydrophilic solution vigorously to form an emulsion, or by any other method conventionally used in the emulsification art. The emulsion comprises microdroplets from the hydrophobic solution that are uniformly dispersed and suspended in the hydrophilic solution. The droplet size and the final size of the matrix particle is controlled by shear rate and degree of agitation, the temperature, the volumetric ratio of the dispersed hydrophobic phase to continuous aqueous phase, and the type of dispersing agent used, if any. Stirring of the emulsion can be continued until all of the organic solvent is evaporated. Once the organic solvent has evaporated, the supernatant liquid can be decanted and the matrix particles can be washed, filtered, and dried or used, preferably as is.

In the process outlined above, the organic solvent used to prepare the hydrophobic solution should be suitable for co-dissolving the required amounts of the active and polymer to form a hydrophobic (water-immiscible) solution. The organic solvent should not otherwise interact with or alter the intended functions of the active or polymer in the prepared matrix particles. The organic solvent should also have adequate volatility at room temperature (sufficiently low boiling point at ambient pressures) in order to evaporate at a reasonable rate from the emulsion. The solvent in the method of the present invention is preferably a substantially hydrophobic solvent. For example, the solvent can comprise a compound selected from the group consisting of halogenated hydrocarbons, aromatic compounds, hydrocarbons, ethers, and esters. Methylene



chloride is an example of an organic solvent suitable for the practice of this invention. Other suitable organic solvents include but are not limited to ethyl acetate, chloroform, carbon tetrachloride, acetonitrile, diethyl  
5 ether, dimethyl ether, acetone, methylethylketone, pentane, hexane, hexanes, heptane, dioxane, ethanol, methanol, pyridine, propanol, 2-propanol, butanol, 2-butanol, t-butyl alcohol, isobutyl alcohol, perchloroethylene, tetrachloroethane, o-xylene, m-xylene, p-xylene, toluene,  
10 benzene, mesitylene, chlorobenzene, o-dichlorobenzene, m-dichlorobenzene, p-dichlorobenzene, or any other organic solvent which is chemically unreactive under the particle-forming conditions and which is capable of being evaporated under temperature or pressure conditions under which the  
15 particle of the present invention is stable. Preferably the solvent comprises a compound selected from the group consisting of methylene chloride, o-xylene, m-xylene, p-xylene, toluene, and chlorobenzene. More preferably the solvent comprises methylene chloride. The amount of  
20 organic solvent useful in forming the hydrophobic solution ranges from about two to about eight times, and preferably about three times, the weight of the polymer (or of the combined weight of the polymer and the active).

In general, no adjustment of the pH of the system is  
25 required during the matrix particle process to achieve satisfactory performance and production of entrapped material.

A preferred process for producing matrix particle of the present invention utilizes solvent evaporation.  
30 Briefly, the solvent evaporation technique involves mixing a hydrophobic liquid medium and a hydrophilic liquid medium

to produce an emulsion. An emulsion can be made with a hydrophobic phase in a hydrophilic phase (e.g., oil-in-water) or with a hydrophilic phase in a hydrophobic phase (e.g., water-in-oil); the former is currently preferred.

5 Moreover, it is preferred to produce an emulsion in which the volume of the hydrophilic phase is significant excess to the volume of the hydrophobic phase. An active ingredient can be added that preferentially dissolves in the hydrophobic phase, and preferably is substantially

10 insoluble in the hydrophilic phase. The shear rate and time period for mixing the hydrophobic and hydrophilic phases is selected so as to produce uniformly dispersed hydrophobic droplets having average diameters in the range from about 0.2 to 200 microns, preferably from about 1 to

15 about 50 microns. The solvent is then evaporated from the hydrophobic phase, producing matrix particles of the present invention.

In the solvent partition technique, an active ingredient is dissolved or dispersed in a volatile organic

20 solvent. The resulting solution is suspended as a fine dispersion in an organic oil into which the organic solvent is extracted to produce particles. This technique can be carried out at room temperature and does not require water. As one example, a polymer is dissolved in methylene

25 chloride, the required amount of an active ingredient (e.g., a fungicide) is added, and the mixture is suspended in silicone oil containing a nonionic emulsifier such as Span 85 and additional methylene chloride. After adding the polymer solution to the silicone oil, petroleum ether

30 is added and the mixture is stirred until the matrixed particles have hardened. The particles can be removed by

filtration or centrifugation, washed with petroleum ether, and dried under vacuum. Examples of the solvent partition technique are provided in R. Langer et al., *Polymer* 31:547-555, 1990. Further examples of the solvent partition  
5 technique are provided in *Kirk-Othmer Encyclopedia of Chemical Technology*, fourth edition, vol. 16, Curt Thies.

In hot melt microencapsulation(;), a polymer melt is mixed with the active ingredient, which can be suspended or dissolved therein. The resulting mixture is suspended in a  
10 nonmiscible solvent (for example, silicone oil or olive oil) that is heated about 5°C above the melting point of the polymer while stirring continuously. After an emulsion is formed and stabilized, it is cooled until the particles are solidified. After cooling, the particles are washed by  
15 decantation with petroleum ether to produce a free-flowing powder. In general, the resulting particles are less than about 50 microns in diameter. Examples of the hot melt microencapsulation technique are provided in E. Mathiowitz and R. Langer, *J. Contr. Rel.* 5:13-22, 1987. Further  
20 examples of the hot melt microencapsulation technique are provided in *Microcapsules and Nanoparticles in Medicine and Pharmacy*, ed. M. Donbrow, CRC Press, 1992, pp. 105-107.

In one embodiment, the present invention provides a method of producing a particle wherein the particle  
25 comprises a triazole fungicide in a polymer matrix comprising providing a hydrophobic solution comprising a triazole fungicide, a polymer, and a solvent; mixing the hydrophobic solution and an aqueous medium to produce a dispersion of droplets of the hydrophobic solution in the  
30 aqueous medium; and evaporating the solvent from the dispersion to produce a particle comprising a triazole

2025 RELEASE UNDER E.O. 14176

fungicide in a polymer matrix. Preferably the fungicide is a triazole fungicide such as bitertanol, bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, hexaconazole, imibenconazole, metconazole, myclobutanil, penconazole, propiconazole, tebuconazole, tetraconazole, triadimefon, triadimenol, or triticonazole. More preferably the fungicide is selected from the group consisting of cyproconazole, epoxiconazole, tebuconazole, triadimefon, and triadimenol.

Preferably the polymer is selected from the group consisting of polystyrene-maleic anhydride copolymer or polymethylmethacrylate.

The hydrophobic solution of the present method can comprise a dispersing agent.

The hydrophilic solution in the method of the present invention can also comprise a dispersing agent. Preferably the dispersing agent in the hydrophilic solution is methyl cellulose or polyvinyl alcohol.

The solvent evaporation step of the method of the present invention can comprise applying vacuum, heat, or a combination of vacuum and heat to the dispersion. Alternatively, the solvent evaporation step can comprise lyophilizing the dispersion.

**Application of matrix particles to soil, seed, or plant.** The particle and formulation composition of the present invention can be applied to the soil, where the active ingredient can be released and eventually affect a target pest either directly or indirectly. For example,

the active ingredient can be taken up by a plant, or taken up by or distributed to a part of which is ingested or infested by the pest.

The particle formulation can be applied by any conventional method, including but not limited to: (1) injection of a formulation (e.g., an aqueous suspension of particles) directly into the soil around seeds or in the root zone of developing plants (e.g., injection at a point 2 cm deep and within a 3 cm radius of the plant crown; (2) application as a soil drench to the point at which the soil is at field capacity; (3) application as a foliar spray, preferably in a sufficient volume to thoroughly wet the foliage; and (4) application directly to seeds (i.e., seed treatment). Release of the active ingredient from the particle will provide a desired biological effect in the zone of application or upon uptake of the active ingredient by the plant.

A particle or formulation of the present invention can be applied to seed by any standard seed treatment methodology, for example, by using a Hege 11 Liquid Seed Dresser.

Matrix particles of the present invention can be applied in combination with another active ingredient that is provided as fast- or slow-release formulations. Slow-release matrix particles according to the present invention can also be applied together with a fast-release formulation having the same active ingredient (or with a particle comprising the same active ingredient) in order to achieve, for example, a chemical application regime with an initial high rate of release followed by a slower rate of release over a longer period of time.

The treatment method of the present invention provides, for example a method for the treatment or prophylaxis of a fungal disease in a target plant wherein the method comprises contacting a plant cell, a plant  
5 tissue, or a seed with a particle wherein the particle comprises a triazole fungicide in a polymer matrix. Preferably the treatment method comprises contacting a seed with the particle of the present invention. Preferably the contacting is performed before the seed is planted.

10 Preferably the triazole fungicide is selected from the group consisting of bitertanol, bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, hexaconazole, imibenconazole, metconazole, myclobutanil,  
15 penconazole, propiconazole, tebuconazole, tetraconazole, triadimefon, triadimenol, and triticonazole. More preferably the fungicidal agent is selected from the group consisting of cyproconazole, epoxiconazole, tebuconazole, triadimefon, and triadimenol.

20 The polymer matrix useful in the treatment method of the present invention preferably comprises a polymer selected from the group consisting of poly(methylmethacrylate), poly(lactic acid), a poly(lactic acid-glycolic acid) copolymer, cellulose acetate butyrate,  
25 a poly(styrene), hydroxybutyric acid-hydroxyvaleric acid copolymer, a styrene maleic anhydride copolymer, poly(methylvinyl ether-maleic acid), poly(caprolactone), poly(n-amylmethacrylate), wood rosin, a polyanhydride, a polyorthoester, a poly(cyanoacrylate), poly(dioxanone),  
30 ethyl cellulose, a ethyl vinyl acetate polymer, poly(ethylene glycol), poly(vinylpyrrolidone), an

D01090:11092260

acetylated monoglyceride, an acetylated diglyceride, an  
acetylated triglyceride, poly(phosphazene), chlorinated  
natural rubber, a vinyl polymer, polyvinyl chloride, a  
hydroxyalkylcellulose, polybutadiene, polyurethane, a  
5 vinylidene chloride polymer, a styrene-butadiene copolymer,  
a styrene-acrylic copolymer, an alkylvinylether polymer, a  
cellulose acetate phthalate, an ethyl vinyl phthalate,  
cellulose triacetate, a polyanhydride, a polyglutamate, a  
polyhydroxy butyrate, polyvinyl acetate, a vinyl acetate-  
10 ethylene copolymer, a vinyl acetate-vinylpyrrolidone  
copolymer, an acrylic polymer, an alkyl acrylate polymer,  
an aryl acrylate polymer, an aryl methacrylate polymer, a  
poly(caprolactam), an epoxy resin, a polyamine epoxy resin,  
a polyamide, a polyvinyl alcohol polymer, a polyalkyd  
15 resin, a phenolic resin, an abietic acid resin, a silicone,  
a polyalkylene oxide, and a polyester.

Preferably after the contacting step, the health of  
the target plant is substantially similar to the health of  
a control plant which is substantially free of the fungal  
20 disease and which is free of contact with the triazole  
fungicide. Alternatively, the health of the target plant  
after the contacting step is intermediate between the  
health of a first control plant which is substantially free  
of the fungal disease and which is free of contact with the  
25 triazole fungicide, and the health of a second control  
plant which is substantially free of the fungal disease and  
which is contacted with the triazole fungicide in the  
absence of the polymer matrix.

30

**EXAMPLES**

3.72 g of cyproconazole (96.3% purity; Sandoz Agro, Ltd., Basel, Switzerland) and 14.3 g of polylactic acid (Chronopol 95; Chronopol, Golden, CO) were dissolved in 156 g methylene chloride (Burdick & Jackson, Muskegon, MI) in a glass bottle with shaking to produce a hydrophobic solution.

7.5 g of polyvinyl alcohol (Elvanol 51-05; DuPont, Wilmington, DE) was dissolved with stirring in deionized water to produce 1500 g of hydrophilic solution.

The hydrophobic solution was added to the hydrophilic solution and the mixture was vigorously stirred to produce an emulsion. The stirring continued for one hour. Microscopic examination of the appearance and size of the oil droplets in the emulsion showed that the average size of oil droplets was in the 30-50 micrometer (micron,  $\mu$ ) range.

The emulsion was then transferred to a two liter (L) round bottom flask and attached to a rotary evaporator to remove the methylene chloride at a reduced pressure. The final methylene chloride residue was removed by heating the flask in a hot water bath at 40°C while on the evaporator.

The resulting particle suspension was filtered on a Buechner funnel to produce a filter cake, which was washed  
25 with three portions of deionized water to remove the last traces of aqueous filtrate. The filter cake was then air dried by spreading the product out on a sheet of clean paper.

An aqueous carrier solution was prepared by dissolving  
30 urea (Fischer Scientific, Pittsburgh, PA) and Methocel®  
A15LV (Dow Chemical Co., Midland, MI) in water by stirring.



Urea was added as an anti-freeze and Methocel A15LV as a combined dispersant and non-phytotoxic sticking agent for use in seed treatments. (A clay thickener such as Van Gel<sup>®</sup> B (R.T. Vanderbilt Co., Inc., Norwalk, CT) are optionally added to the aqueous carrier solution to improve viscosity and reduce settling.) The dry microcapsules were stirred into the aqueous carrier solution to produce a homogenous suspension.

The composition of the final formulation (Formulation 1) is shown below.

Formulation 1			
Ingredients	% w/w	Weight (g)	Active Ingredient ("a.i.")
Cyproconazole (19.88%)	17.72	37.32	7.42 g (% a.i. (w/w) = 3.52)
Urea	4.49	9.46	
Methocel <sup>®</sup> A15LV	0.05	1.05	
Water, deionized	77.29	162.79	
<b>Total</b>	100.00%	210.62	% polymer (w/w) = 14.2

#### Example 2

1.56 g cyproconazole (96.3% purity) and 13.44 g cellulose acetate butyrate polymer (Sigma Chemical Co., St. Louis, MO) were dissolved in 82.22 g methylene chloride in a glass bottle with shaking to produce a hydrophobic solution. 1.00 g of Methocel<sup>®</sup> A15LV and 20 g of urea were dissolved in 64 g deionized water to prepare 85 g of a hydrophilic solution. The hydrophobic solution was added to the hydrophilic solution with stirring to produce an emulsion. The emulsion was stirred for 5 minutes to equilibrate. To reduce the particle size further, the emulsion was sonicated for 5.5 minutes with a sonic

dismembrator (Model 550, Fischer Scientific, Pittsburgh, PA) using a variable power range. Cooling was provided by an ice bath to keep the temperature below 30°C. Microscopic examination showed particles mainly in the 4-5 micron range. The emulsion was transferred to a rotary evaporator and methylene chloride stripped off as described in Example 1. The resulting product was passed through a #325 mesh sieve to remove foreign particles and assayed for particle size, density (at room temperature), and % active ingredient.

The following were the properties of the matrix particles (Formulation 2):

**Formulation 2 - Properties**

% active ingredient (w/w)	1.72
Density, g/mL	1.11
Ave. particle size, $\mu$	4.4

**Example 3**

Following the general procedure of Example 2, matrix particle suspensions having the compositions given below were produced. For Formulation 3, methylene chloride was evaporated with stirring at atmospheric pressure. For Formulation 4, Formulation 5, Formulation 6, and Formulation 7, methylene chloride was evaporated with a rotary evaporator at reduced pressure. For Formulation 7, Van Gel<sup>®</sup> B was added as part of the aqueous carrier medium. Poly(methylmethacrylate) (PMM) and polystyrene (50,000 MW) were obtained from Polysciences Inc. (Warrington, PA)

Weight % of Ingredients
-------------------------

Ingredients	Formulation Number				
	3	4	5	6	7
Cyproconazole*	1.50	1.50	3.00	3.00	3.00
Chronopol 95	13.50	13.50	-	-	-
PMM	-	-	6.00	12.00	6.00
Polystyrene	-	-	6.00	-	6.00
Methocel A15LV	1.00	1.00	1.06	1.06	-
Urea	20.00	20.00	-	-	-
Van Gel B	-	-	-	-	3.40
Water	64.00	64.00	83.94	83.94	81.60
Total	100.00	100.00	100.00	100.00	100.00

\*100% a.i. basis. Compensate for purity with polymer.

The matrix particle suspensions had the following properties:

5

Properties	Formulation				
	3	4	5	6	7
Density R.T., g/mL	1.10	1.12	1.02	1.04	1.02
Ave. particle size, $\mu\text{m}$	1.18	2.52	1.84	1.13	138.50
Viscosity* at room temperature, cps	spindle # 18	spindle # 18	spindle # 18	spindle # 18	spindle # 31
R.P.M. - 60	11.30	27.90	9.52	16.70	185
R.P.M. - 30	12.40	28.60	9.92	17.00	329
R.P.M. - 12	15.50	32.60	11.00	17.00	765
R.P.M. - 6	22.00	36.10	13.50	21.00	1520

064050-11032260

\* Viscosity in centipoise (cps) was determined using a Brookfield viscometer (model LVT, Brookfield Engineering Laboratories, Stoughton, MA) according to manufacturer instructions).

#### 5 Example 4

Following the general procedure of Example 2, matrix particle suspensions having the compositions given below were produced:

Ingredients	Weight % of Ingredients		
	Formulation		
	5	8	9
Cyproconazole*	3.00	3.00	3.00
Chronopol 95	-	-	6.00
PMM	6.00	6.00	-
Polystyrene	6.00	6.00	6.00
Methocel A15LV	1.06	1.00	1.00
Van Gel B	-	2.06	2.06
Water	83.94	81.94	83.94
Total	100.00	100.00	100.00

\* 100 % a.i. basis. Compensate for purity with polymer.

10

The matrix particle suspensions were analyzed for the following properties:

Properties	Formulation		
	5	8	9
Density, R.T., g/mL	1.02	1.04	1.04
Ave. particle size, $\mu$	1.84	2.06	6.15
Viscosity at room temperature, cps	spindle # 18	spindle # 18	spindle # 18
R. P. M.* - 60	9.52	22.70	21.70
R. P. M.* - 30	9.92	26.20	22.90
R. P. M.* - 12	11.00	34.60	25.40
R. P. M.* - 6	13.50	41.60	27.00

15 \* Revolutions per minute.

000050-4T092E60

**Example 5**

Following the general procedure of Example 2, matrix particle suspensions having the compositions given below were produced. The hydrophilic and hydrophobic solutions were sonicated to produce an emulsion for preparation of Formulation 8 and homogenized with a Silverson L4R laboratory homogenizer (Silverson Machines, Inc., East Longmeadow, MA) to produce an emulsion for preparation of Formulation 10 and Formulation 11.

Ingredients	Weight % of Ingredients		
	Formulation		
	8	10	11
Cyproconazole*	3.00	3.00	3.00
PMM	6.00	6.00	6.00
Polystyrene	6.00	6.00	6.00
Methocel A15LV	1.00	1.00	1.00
Van Gel B	2.06	2.06	3.00
Water	81.94	81.94	81.00
Total	100.00	100.00	100.00

\* 100 % a.i. basis. Compensate for purity with polymer.

The matrix particle suspensions had the following properties:

Properties	Formulation		
	8	10	11
Density, R.T., g/ml	1.04	1.04	1.05
Ave. particle size, $\mu\text{m}$	2.06	3.55	3.20
Viscosity at room temperature, cps	spindle # 18	spindle # 18	spindle # 31
R.P.M. - 60	22.70	47.40	192
R.P.M. - 30	26.20	52.40	265
R.P.M. - 12	34.60	61.80	446
R.P.M. - 6	41.60	74.60	685

<sup>a</sup>Gel structure.

**Example 6**

Following the general procedure of Example 2, matrix particle suspensions having the compositions in the table below were produced. The hydrophilic and hydrophobic solutions were homogenized in a cooling bath in preparing Formulation 12 and Formulation 13, but not in preparing Formulation 10 and Formulation 14.

Ingredients	Weight % of Ingredients			
	Formulation			
	10	14	12	13
Cyproconazole*	3.00	3.00	3.00	3.00
PMM	6.00	6.00	6.00	6.00
Polystyrene	6.00	6.00	6.00	6.00
Methocel A15 C	-	0.75	1.75	0.75
Methocel A15LV	1.00	-	-	-
Van Gel B	2.06	-	-	-
Water	81.94	84.25	83.25	84.25
Total	100.00	100.00	100.00	100.00

\* 100 % a.i. basis. Compensate for purity with polymer

10

The matrix particle suspensions were analyzed for the following properties:



\*\* (1) Chronopol 95; (2) cellulose acetate butyrate; (3) poly (methyl methacrylate).

The matrix particle suspension were analyzed for the  
5 following properties:

Properties	Formulation				
	15	16	17	18	19
% a.i.	3.19	3.62	3.47	4.41	3.53
Ave. particle size, $\mu\text{m}$	40.00	193.00	75.00	22.80	70.00

The formulations produced in this Example were applied to wheat as follows. Wheat seed was weighed out into 50 g batches for each treatment. Stock solutions were prepared by weighing out the formulation and adding deionized water to prepare stock solutions of the high rate for each formulation, then, dilutions were prepared from these stocks to provide various rates of application.

15           A Hege 11 laboratory scale rotostatic seed treater  
with a 200-gram small capacity seed treatment drum was  
used for the seed treatments.

For each treatment, a sample batch of seed was treated with the formulation or with the solvent alone to wet up/dirty the drum as recommended by the manufacturer. This seed sample was then discarded. The treatment was then drawn up into a syringe and slowly applied to a new 50 g batch of seed in the seed treater. As soon as the seed appeared dry (usually about 30-45 seconds), it was transferred into a 1 L plastic beaker. The seed was then transferred to a 4 oz. glass jar for storage. The lid of the jar was left off for several hours to ensure that the



seed was totally dry. The treatments were applied in order from the lowest rate to the highest rate for each formulation. After the highest rate for each formulation, the seed treater was thoroughly scrubbed out with absolute  
5 ethanol on a paper tissue to prevent contamination of the next formulation. The syringe, funnel and beaker were also rinsed with ethanol. This procedure was repeated for each of the formulations that were tested.

At the end of all the treatments and/or when active  
10 ingredients were changed in the course of the same study, we also used an additional step of cleaning with a solution of soap in water and an additional ethanol wipe.

In order to assess the safety of the formulations, wheat seed that had been treated previously with test  
15 formulations was seeded in standard 4"-square pots containing sterilized Dupo silt loam soil. Seeding was done at a rate of 12-25 seeds per pot, with four replicate pots of each treatment rate. Seeds were covered with approximately 2 cm of the same soil and incubated under a  
20 12-hour photoperiod, 50% relative humidity at 18°C. Eight to twelve days after planting (DAP), each replicate pot of each treatment was rated for the number of seedlings emerged and the average height of emerged seedlings was estimated. The main indicator of formulation performance  
25 was the measure of seedling height relative to untreated control plants (untreated = 100%).

The table below shows and Fig. 1 illustrates the safety of these treatments, expressed as the height of germinating wheat at 9 days after planting (DAP) as a  
30 percent of the height of untreated controls. For comparison, Alto 005LS (Sandoz Agro, Ltd., Basel,

002204 05040900 002204

Switzerland) was included as a standard, fast-release non-matrix formulation liquid seed treatment of cyproconazole.

Rep. No.	Formulation	Intended Rate (g/100 kg Seed)	Analytical Percent Recovery of Applied	Predicted Rate (g a.i./100 kg seed)	Height of Treated Plant in cm (9 DAP)	Percent of Control Height (9 DAP)
1-1	ALTO 005LS	1.1			9.6	82
1-2	ALTO 005LS	4.4	98.4	4.3296	7.5	64
1-3	ALTO 005LS	8.8	93.1	8.1928	6.5	55
1-4	ALTO 005LS	17.6	90.5	15.928	4.0	33.5
1-5	15	1.1			10.4	88.6
1-6	15	4.4	75.7	3.3308	9.0	76.5
1-7	15	8.8	75.6	6.6528	8.5	72.5
1-8	15	17.6	70.5	12.408	8.4	71.5
1-9	15	35.2	261	91.872	3.7	31.6
1-10	18	1.1			10.8	92
1-11	18	4.4	79.8	3.5112	9.4	79.8
1-12	18	8.8	83.6	7.3568	9.4	80.3
1-13	18	17.6	97	17.072	8.1	68.5
1-14	19	1.1			11.5	98
1-15	19	4.4	66.6	2.9304	10.2	86.9
1-16	19	8.8	63.2	5.5616	9.7	82.6
1-17	19	17.6	67	11.792	8.6	73.4
1-18	16	1.1			10.1	86.3
1-19	16	4.4	76.6	3.3704	10.1	85.6
1-20	16	8.8	67.7	5.9576	9.3	79.2
1-21	16	17.6	65.1	11.4576	9.0	76.1
1-22	17	1.1			10.5	89.2
1-23	17	4.4	89.8	3.9512	9.6	81.3
1-24	17	8.8	101	8.888	8.9	75.3
1-25	17	17.6	90.5	15.928	8.7	73.6
1-26	82	1.1			9.2	78.6
1-27	82	4.4	106.1	4.6684	8.2	69.4
1-28	82	8.8	101.1	8.8968	7.0	59.4
1-29	82	17.6	98.4	17.3184	5.7	48

001050" 11092250

1-30	Untreated Check	0			9.2	100
------	--------------------	---	--	--	-----	-----

**Example 8**

Following the general procedure of Example 2, matrix particle suspensions having the following compositions were produced. Cellulose acetate butyrate was obtained from Sigma Chemical Co. (St. Louis, MO). SMA 1440A resin, an ester/styrene maleic anhydride copolymer, was obtained from Sartomer Co. (West Chester, PA). Poly(methyl vinyl ether/maleic acid) was obtained from Sigma Chemical Co. (St. Louis, MO).

10

Ingredients	Weight % of Ingredients				
	Formulation				
	20	21	22	23	24
Cyproconazole*	1.50	1.50	1.50	1.50	1.50
Cellulose acetate butyrate	6.75	-	-	6.75	-
SMA <sup>®</sup> 1440A Resin	6.75	13.50		-	-
Wood rosin	-	-	13.50	-	-
Poly (methyl vinyl ether/maleic acid)	-	-	-	6.75	-
PMM	-	-	-	-	13.50
Methocel A15C	1.00	1.00	1.00	1.00	1.00
Water	84.00	84.00	84.00	84.00	84.00
Total	100.00	100.00	100.00	100.00	100.00

\*100 % a.i. basis. Compensate for purity with polymer

The suspensions produced in this Example were applied to wheat using the procedure set forth in Example 7. The table below shows and Fig. 2 illustrates the safety of

these treatments at 10 days after planting as compared to Alto 005LS.

Rep. No.	Formulation	Inten- ded Rate (g/100 kg Seed)	Analytical Percent Recovery of Applied	Predicted Rate (g a.i./100 kg seed)	Height of Treated Plant in cm (9 DAP)	Percent of Control Height (9 DAP)
2-1	ALTO 005LS	1.1	122.7	1.35	8.2	80.4
2-2	ALTO 005LS	4.4	114.1	5.02	6.6	64.9
2-3	ALTO 005LS	8.8	91	8.01	5.0	49.0
2-4	ALTO 005LS	17.6	93.7	16.49	3.5	34.5
2-5	20	1.1	81.3	0.89	9.0	87.9
2-6	20	4.4	85.2	3.75	8.0	78.4
2-7	20	8.8	78.2	6.88	7.3	70.7
2-8	20	17.6	73.2	12.88	6.2	60.2
2-9	21	1.1	91.8	1.01	9.0	87.8
2-10	21	4.4	68.4	3.01	7.8	76.4
2-11	21	8.8	75.2	6.62	7.1	69.1
2-12	21	17.6	83	14.61	5.0	49.1
2-13	22	1.1	80.9	0.89	8.7	84.6
2-14	22	4.4	70.2	3.09	7.5	72.7
2-15	22	8.8	76	6.69	6.8	66.2
2-16	22	17.6	78.9	13.89	5.3	51.9
2-17	23	1.1	120	1.32	8.3	80.9
2-18	23	4.4	98.9	4.35	7.5	73.4
2-19	23	8.8	62.7	5.52	7.3	71.3
2-20	23	17.6	99.3	17.48	4.4	42.3
2-21	24	1.1	240	2.64	8.6	83.7
2-22	24	4.4	124.5	5.48	8.5	83.3
2-23	24	8.8	126	11.09	7.5	73.3
2-24	24	17.6	109	19.18	7.7	75.3
2-25	Untreated Check	0	0		10.3	100.0

[illegible]

**Example 9**

Following the general procedure of Example 1, matrix particle suspensions having the following compositions were produced. Lactel BP-400 was obtained from Sigmal Chemical Co. (St. Louis, MO).

Ingredients	Weight % of Ingredients	
	Formulations	
	25	26
Cyproconazole*	3.0	3.0
Lactel BP-400	-	12.0
Cellulose acetate butyrate	12.0	-
Methocel A15LV	1.0	1.0
Water	84.0	84.0
Total	100.0	100.0

\* 100 % a.i. basis. Compensate for purity with polymer.

The suspensions produced in this Example were applied to wheat using the procedure set forth in Example 7. The table below shows and Fig. 3 illustrates the safety of these treatments at 10 days after planting as compared to Alto 005LS.

Rep. No.	Rate (g a.i./ 100 kg seed)	Formulation	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
3-1	1	ALTO 005LS	7.88	74.4
3-2	4	ALTO 005LS	5.33	50.4
3-3	8	ALTO 005LS	2.75	26.0
3-4	16	ALTO 005LS	0.83	7.8
3-5	1	25	10.95	103.7
3-6	4	25	10.25	97.0
3-7	8	25	9.88	93.5
3-8	16	25	9.20	87.1
3-9	1	26	9.67	91.7
3-10	4	26	9.00	85.2

3-11	8	26	9.68	91.5
3-12	16	26	8.70	82.3
3-13	1	88	8.25	78.1
3-14	4	88	6.75	63.9
3-15	8	88	5.55	52.7
3-16	16	88	4.3	40.8
3-17	1	89	7.85	74.3
3-18	4	89	6.25	59.2
3-19	8	89	4.93	46.6
3-20	16	89	3.68	34.8
3-21	1	90	8.43	79.6
3-22	4	90	6.53	61.8
3-23	8	90	5.00	47.3
3-24	16	90	3.68	34.8
3-25	1	91	7.85	74.3
3-26	4	91	6.60	62.4
3-27	8	91	5.15	48.7
3-28	16	91	3.40	32.2
3-29	0	Control (Caldwell 96 (B-H52) )	10.58	100.0

**Example 10**

Following the general procedure of Example 1, matrix particle suspensions having the following compositions were produced.

Ingredients	Weight % of Ingredients	
	Formulation	
	27	28
Cyproconazole*	3.00	3.00
Chronopol 95	10.92	6.12
Polystyrene	1.20	6.00
Methocel A15LV	1.56	1.61
Water	83.32	83.27
Total	100.00	100.00

\* 100 % a.i. basis. Compensate for purity with polymer.

5 Alto 005LS.

Rep. No.	Rate (g a.i./ 100 kg seed)	Formulation	Height of Treated Plant in cm (11 DAP)	Percent of Control Height (11 DAP)
4-1	1	51	8.4	72.6
4-2	4	51	7.0	60.6
4-3	8	51	6.7	57.4
4-4	16	51	4.8	41.6
4-5	1	47	9.5	82.1
4-6	4	47	7.7	66.4
4-7	8	47	6.1	52.2
4-8	16	47	3.8	32.8
4-9	1	48	9.7	83.2
4-10	4	48	8.5	73.1
4-11	8	48	6.8	58.9
4-12	16	48	5.5	47.4
4-13	1	ALTO 005LS	9.1	78.2
4-14	4	ALTO 005LS	7.3	63.1
4-15	8	ALTO 005LS	5.5	47.0
4-16	16	ALTO 005LS	3.0	25.9
4-17	1	5932801A2	10.8	92.9
4-18	4	5932801A2	9.7	83.9
4-19	8	5932801A2	9.3	80.0
4-20	16	5932801A2	8.6	74.1
4-21	1	5932801B2	10.8	93.1
4-22	4	5932801B2	10.1	86.9
4-23	8	5932801B2	8.9	77.0
4-24	16	5932801B2	8.6	73.9

4-25	0	Control (96 Caldwell (B- H52))	11.6	100.0
------	---	--------------------------------------	------	-------

**Example 11**

Following the general procedure of Example 1, matrix particle suspensions having the following compositions were produced.

5

Ingredients	Weight % of Ingredients		
	Formulation		
	29	30	93
Cyproconazole*	20.1	3.04	3.71
Chronopol 95	79.9	10.41	8.67
Methocel A15LV	-	1.27	1.09
Water	-	85.28	86.53
Total	100.0	100.0	100.0

\* 100 % a.i. basis. Compensate for purity with polymer.

The following procedure was used to prepare a matrix  
 10 particle suspension having the composition in the table  
 below. A 38.5% by weight a.i. suspension of cyproconazole  
 was prepared using a laboratory mill. The particles were  
 milled to an average size of less than 10 microns in  
 diameter. Separately, a solution was prepared containing  
 15 3.82% by weight of alginic acid and 0.15% by weight of  
 calcium acetate in water. The cyproconazole solution was  
 warmed to 50 C with stirring. The alginic acid/calcium  
 acetate was warmed to 60 C with stirring. The  
 cyproconazole suspension was poured rapidly into the  
 20 stirring alginic acid solution. The resultant mixture was  
 stirred until it equilibrated to room temperature (about 2  
 hours). The mixture was poured through a #50 mesh sieve  
 and bottled.

067050" 77052260



Ingredients	Weight % of Ingredients	
	Formulation	
	82	
Cyproconazole*	14.05	
Morwet D-425	1.83	
Calcium Acetate	0.10	
Alginic Acid	2.42	
Water	81.60	
Total	100.0	

\* 100 % a.i. basis. Compensate for purity with polymer.

5

The suspensions produced in this Example were applied to wheat using the procedure set forth in Example 7. The table below shows and Fig. 5 illustrates the safety of Formulation 29 at 10 days after planting (DAP) as compared to Alto 005LS.

10

Data Corresponding to Fig. 5

Rep. No.	Formulation	Rate (g a.i./ 100 kg seed)	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
5-1	ALTO 005LS	1	8.08	79.1
5-2	ALTO 005LS	2	7.33	71.6
5-3	ALTO 005LS	4	5.63	55.0
5-4	ALTO 005LS	8	4.15	40.5
5-5	29	1	8.13	79.5
5-6	29	2	8.38	81.9
5-7	29	4	8.10	79.3
5-8	29	8	8.80	86.1
5-9	35	1	10.50	102.7
5-10	35	2	9.43	92.2
5-11	35	4	8.95	87.6
5-12	35	8	8.08	79.0
5-13	Untreated	0	10.23	100.0

000090" 11092260

	Check			
--	-------	--	--	--

The table below shows and Fig. 6 illustrates the safety of Formulation 30 at 10 days after planting (DAP) as compared to Alto 005LS.

5

Data Corresponding to Fig. 6

Rep. No.	Formulation	Intended Application Rate (g a.i./100 kg seed)	Analytical Percent Recovery of Applied	Predicted Rate (g a.i./100 kg seed)	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
6-1	97	1.1	69	0.76	8.63	79.63
6-2	97	4.4	81.4	3.58	7.05	65.02
6-3	97	8.8	83	7.30	5.68	52.33
6-4	97	17.6	79.7	14.03	3.98	36.85
6-5	49	1.1	19.1	0.21	10.73	98.80
6-6	49	4.4	13.1	0.58	10.03	92.48
6-7	49	8.8	11.6	1.02	9.80	90.33
6-8	49	17.6	19	3.34	9.08	83.70
6-9	30	1.1	32.7	0.36	10.25	94.40
6-10	30	4.4	22.6	0.99	8.60	79.40
6-11	30	8.8	21.5	1.89	8.45	78.03
6-12	30	17.6	19.5	3.43	8.33	76.70
6-13	31	1.1	100.9	1.11	9.93	91.35
6-14	31	4.4	87.3	3.84	8.80	81.30
6-15	31	8.8	134.9	11.87	8.53	78.63
6-16	31	17.6	116.9	20.57	7.23	66.53
6-17	93	1.1	79.1	0.87	8.55	78.65
6-18	93	4.4	73.2	3.22	7.25	67.18
6-19	93	8.8	56.9	5.01	6.40	59.08
6-20	93	17.6	46.6	8.20	6.60	61.03
6-25	1	1.1	47.3	0.52	9.80	90.40
6-26	1	4.4	42.5	1.87	8.70	80.23
6-27	1	8.8	54.4	4.79	7.95	73.38
6-28	1	17.6	48.8	8.59	7.38	67.70
6-29	82	1.1	86.4	0.95	7.90	73.05
6-30	82	4.4	80.7	3.55	6.95	64.18
6-31	82	8.8	78.4	6.90	5.15	47.08
6-32	82	17.6	54	9.50	5.08	46.40
6-33	ALTO	1.1	122.7	1.35	8.05	74.30

667050-17092260

	005LS					
6-34	ALTO 005LS	4.4	90.2	3.97	6.23	57.45
6-35	ALTO 005LS	8.8	95.6	8.41	3.83	35.50
6-36	ALTO 005LS	17.6	89.2	15.70	2.18	20.10
6-37	Untreated Check	0		0.00	10.88	100.00

**Example 12**

Following the general procedure of Example 1, matrix  
 5 particle suspensions having the following compositions were  
 produced.

Ingredients	Weight % of Ingredients		
	Formulation		
	30	31	32
Cyproconazole*	3.04	22.3	30
Chronopol 95	10.41	77.7	70
Methocel A15LV	1.27		
Water	85.28		
Total	100	100.0	100

\* 100 % a.i. basis. Compensate for purity with  
 polymer.

10

The suspensions produced in this Example were applied  
 to wheat using the procedure set forth in Example 7. The  
 data in the table below show and Fig. 7 illustrates the  
 safety of Formulation 30 and Formulation 31 at 10 days  
 15 after planting as compared to Alto 005LS.

Rep. No.	Formulation	Intended Application Rate (g a.i./100 kg seed)	Analytical Percent Recovery of Applied	Predicted Rate (g a.i./100 kg seed)	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
6-1	97	1.1	69	0.76	8.63	79.63
6-2	97	4.4	81.4	3.58	7.05	65.02
6-3	97	8.8	83	7.30	5.68	52.33
6-4	97	17.6	79.7	14.03	3.98	36.85
6-5	49	1.1	19.1	0.21	10.73	98.80
6-6	49	4.4	13.1	0.58	10.03	92.48
6-7	49	8.8	11.6	1.02	9.80	90.33
6-8	49	17.6	19	3.34	9.08	83.70
6-9	30	1.1	32.7	0.36	10.25	94.40
6-10	30	4.4	22.6	0.99	8.60	79.40
6-11	30	8.8	21.5	1.89	8.45	78.03
6-12	30	17.6	19.5	3.43	8.33	76.70
6-13	31	1.1	100.9	1.11	9.93	91.35
6-14	31	4.4	87.3	3.84	8.80	81.30
6-15	31	8.8	134.9	11.87	8.53	78.63
6-16	31	17.6	116.9	20.57	7.23	66.53
6-17	93	1.1	79.1	0.87	8.55	78.65
6-18	93	4.4	73.2	3.22	7.25	67.18
6-19	93	8.8	56.9	5.01	6.40	59.08
6-20	93	17.6	46.6	8.20	6.60	61.03
6-25	1	1.1	47.3	0.52	9.80	90.40
6-26	1	4.4	42.5	1.87	8.70	80.23
6-27	1	8.8	54.4	4.79	7.95	73.38
6-28	1	17.6	48.8	8.59	7.38	67.70
6-29	82	1.1	86.4	0.95	7.90	73.05
6-30	82	4.4	80.7	3.55	6.95	64.18
6-31	82	8.8	78.4	6.90	5.15	47.08
6-32	82	17.6	54	9.50	5.08	46.40
6-33	ALTO 005LS	1.1	122.7	1.35	8.05	74.30
6-34	ALTO 005LS	4.4	90.2	3.97	6.23	57.45
6-35	ALTO 005LS	8.8	95.6	8.41	3.83	35.50
6-36	ALTO 005LS	17.6	89.2	15.70	2.18	20.10
6-37	Untreated Check	0		0.00	10.88	100.00

667090" 11092260

The table below show and Fig. 8 illustrates the safety of Formulation 31 and Formulation 32 at 10 days after planting as compared to Alto 005LS.

Rep. No.	Form-ulation	Rate (g a.i./ 100 kg seed)	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
8-1	ALTO 005LS	1	8.63	88.6
8-2	ALTO 005LS	2	8.25	84.7
8-3	ALTO 005LS	4	7.43	76.3
8-4	ALTO 005LS	8	6.38	65.6
8-5	31	1	9.50	97.8
8-6	31	2	8.90	91.4
8-7	31	4	9.38	96.3
8-8	31	8	9.88	101.4
8-9	32	1	9.95	102.2
8-10	32	2	9.75	100.2
8-11	32	4	9.75	100.2
8-12	32	8	10.15	104.3
8-13	Untreated Check	0	9.75	100

5

### Example 13

Following the general procedure of Example 1 and using the ingredients which are listed below matrix particle suspensions having the following compositions were produced. Biopol D400G was obtained from Monsanto Company (St. Louis, MO). Polyvinylpyrrolidone/vinyl acetate copolymer (PVP/VA S-630), which was used as a dispersant, was obtained from GAF Chemicals Corp. (Wayne, NJ).

15

601050-11092260

Ingredients	Weight % of Ingredients		
	Formulation		
	33	34	35
Cyproconazole*	10	22.3	22.3
Biopol D400G	-	77.7	-
Chronopol 95 + inerts	90	-	77.7**
Total	100	100.0	100.0

\* 100% a.i. basis. Compensate for purity with polymer and inerts.

The suspensions produced in this Example were applied to wheat using the procedure set forth in Example 7. The data in the table below show and Fig. 9 illustrates the safety of Formulation 33 and Formulation 34 at 10 days after planting as compared to Alto 005LS.

Rep. No.	Formulation	Rate (g a.i./ 100 kg seed)	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
9-1	ALTO 005LS	1	8.63	88.6
9-2	ALTO 005LS	2	8.25	84.7
9-3	ALTO 005LS	4	7.43	76.3
9-4	ALTO 005LS	8	6.38	65.6
9-5	33	1	9.50	97.5
9-6	33	2	9.63	98.9
9-7	33	4	9.38	96.3
9-8	33	8	8.75	90
9-9	34	1	10.25	105.4
9-10	34	2	8.50	87.3
9-11	34	4	8.63	88.6
9-12	34	8	10.05	103.1
9-13	Untreated Check	0	9.75	100

000050-11092260

The data in the table below show and Fig. 10 illustrates the safety of Formulation 35 at 10 days after planting as compared to Alto 005LS.

Rep. No.	Formulation	Rate (g a.i./ 100 kg seed)	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
5-1	ALTO 005LS	1	8.08	79.1
5-2	ALTO 005LS	2	7.33	71.6
5-3	ALTO 005LS	4	5.63	55.0
5-4	ALTO 005LS	8	4.15	40.5
5-5	29	1	8.13	79.5
5-6	29	2	8.38	81.9
5-7	29	4	8.10	79.3
5-8	29	8	8.80	86.1
5-9	35	1	10.50	102.7
5-10	35	2	9.43	92.2
5-11	35	4	8.95	87.6
5-12	35	8	8.08	79.0
5-13	Untreated Check	0	10.23	100.0

5

#### Example 14

Following the general procedure of Example 1 matrix particle suspensions having the following compositions were produced.

10

Ingredients	Weight % of Ingredients		
	Formulation		
	36	37	38
Cyproconazole	*3.17	*3.01	*3.01
Elvanol 51-05	1.64	1.26	1.26
Methocel A15LV	-	-	-
Chronopol 50	11.06	-	-
Chronopol 95	-	10.43	-
Chronopol 100	-	-	10.43
Water	84.13	85.30	85.30
Total	100.00	100.00	100.00

The suspensions produced in this Example were applied to wheat using the procedure set forth in Example 7. The data in the table below show and Fig. 11 illustrates the safety of these suspensions at 10 days after planting as compared to Alto 005LS.

Rep. No.	Form-ulation	Rate (g a.i./ 100 kg seed)	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
11-1	ALTO 005LS	1	10.75	78.2
11-2	ALTO 005LS	2	8.88	64.5
11-3	ALTO 005LS	4	8.25	60.0
11-4	ALTO 005LS	8	6.38	46.4
11-5	38	1	12.75	92.7
11-6	38	2	12.25	89.1
11-7	38	4	10.88	79.1
11-8	38	8	9.88	71.8
11-9	36	1	12.13	88.2
11-10	36	2	12.13	88.2
11-11	36	4	11.25	81.8
11-12	36	8	9.75	70.9
11-13	40	1	12.25	89.1
11-14	40	2	11.00	80.0
11-15	40	4	9.88	71.8
11-16	40	8	9.00	65.5
11-17	39	1	11.63	84.5
11-18	39	2	11.88	86.4
11-19	39	4	11.00	80.0
11-20	39	8	10.00	72.7
11-21	30	1	13.50	98.2
11-22	30	2	12.88	93.6
11-23	30	4	12.38	90.0
11-24	30	8	10.50	76.4
11-25	37	1	13.13	95.5
11-26	37	2	13.13	95.5
11-27	37	4	11.75	85.5
11-28	37	8	10.50	76.4

007050" 11092260



11-29	Untreated Check	0	13.75	100.0
-------	--------------------	---	-------	-------

**Example 15**

Following the general procedure of Example 1 and using  
 5 the ingredients which are listed below matrix particle  
 suspensions having the following compositions were  
 produced.

Ingredients	Weight % of Ingredients		
	Formulation		
	39	30	40
Cyproconazole*	3.05	3.04	3.04
Elvanol 51-05	-	-	-
Methocel A15LV	1.25	1.27	1.27
Chronopol 50	10.40	-	-
Chronopol 95	-	10.41	-
Chronopol 100	-	-	10.41
Water	85.30	85.28	85.28
Total	100.00	100.00	100.00

\* 100% a.i. basis. Compensate for purity with polymer  
 and inerts.

10

The suspensions produced in this Example were applied to  
 wheat using the procedure set forth in Example 7. The data  
 in the table below show and Fig. 12 illustrates the safety  
 15 of these compounds at 10 days after planting as compared to  
 Alto 005LS.

Rep. No.	Form- ulation	Rate (g a.i./ 100 kg seed)	Height of Treated Plant in cm (10 DAP)	Percent of Control Height (10 DAP)
11-1	ALTO 005LS	1	10.75	78.2
11-2	ALTO	2	8.88	64.5

001050-1F092260

	005LS			
11-3	ALTO 005LS	4	8.25	60.0
11-4	ALTO 005LS	8	6.38	46.4
11-5	38	1	12.75	92.7
11-6	38	2	12.25	89.1
11-7	38	4	10.88	79.1
11-8	38	8	9.88	71.8
11-9	36	1	12.13	88.2
11-10	36	2	12.13	88.2
11-11	36	4	11.25	81.8
11-12	36	8	9.75	70.9
11-13	40	1	12.25	89.1
11-14	40	2	11.00	80.0
11-15	40	4	9.88	71.8
11-16	40	8	9.00	65.5
11-17	39	1	11.63	84.5
11-18	39	2	11.88	86.4
11-19	39	4	11.00	80.0
11-20	39	8	10.00	72.7
11-21	30	1	13.50	98.2
11-22	30	2	12.88	93.6
11-23	30	4	12.38	90.0
11-24	30	8	10.50	76.4
11-25	37	1	13.13	95.5
11-26	37	2	13.13	95.5
11-27	37	4	11.75	85.5
11-28	37	8	10.50	76.4
11-29	Untreated Check	0	13.75	100.0

**Example 16**

Following the general procedure of Example 2 matrix particle suspensions having the following compositions were produced. Lucite #29 was obtained from Polysciences Inc. (Warrington, PA).

Weight % of Ingredients
-------------------------

Ingredients	Formulation	
	41	42
Cyproconazole*	2.95	1.48
Lucite #29	11.80	-
Cellulose acetate butyrate	-	13.27
Methocel A15LV	1.00	1.00
Water	84.25	84.25
Total	100.00	100.00

\* 100 % a.i. basis. Compensate for purity with polymer.

The suspensions produced in this Example were applied to wheat using the procedure set forth in Example 7. The data in the table below show and Fig. 13 illustrates the safety of these compounds at 10 days after planting as compared to Alto 005LS.

Rep. No.	Formulation	Rate (g a.i./ 100 kg seed)	Analytical Percent Recovery of Applied	Predicted Rate (g a.i./ 100 kg seed)	Avg. No. of Plants Germinating (out of 12)	Height of Treated Plant in cm (9 DAP)	% of Control Height (9 DAP)
13-1	ALTO 005LS	4.4	98.4	4.3	11.25	8.5	73.7
13-2	ALTO 005LS	8.8	93.1	8.2	7.5	5.6	48
13-3	ALTO 005LS	17.6	90.5	15.9	3.25	5.	42.6
13-8	42	4.4	38.2	1.85	10.25	11.3	97.6
13-9	42	8.8	61.9	5.99	11.25	10.2	88
13-10	42	17.6	72.8	14.09	11.25	9.4	81.2
13-11	42	35.2	81.6	31.6	11.75	8.9	76.9
13-16	41	4.4	68.4	3.31	10.25	11.	94.6
13-17	41	8.8	77.7	7.52	11.5	10.	86.2
13-18	41	17.6	83.9	16.24	11	10.	86.3
13-19	41	35.2	91.4	35.39	11.75	8.8	75.4
13-20	24	4.4	123.2	5.96	11.5	10.1	86.6
13-21	24	8.8	120.9	11.7	8.25	8.4	72.1
13-22	24	17.6	111.9	21.66	9.75	9.5	82.1
13-23	24	35.2	138.6	53.67	11.25	8.7	74.6

13-24	UN-TREATED CHECK	0			12	11.6	100
-------	---------------------	---	--	--	----	------	-----

**Example 17**

Following the general procedure of Example 2, a matrix particle suspension having the following composition and properties was produced. Tebuconazole was obtained from Bayer (Leverkusen, Germany).

Formulation 43	
Ingredients	% w/w
Tebuconazole*	3.52
Chronopol 95	14.35
Urea	4.49
Methocel A15LV	0.50
Water	77.14
Total	100.0

Property	
Tebuconazole* (Wt %)	3.37
Density, g/mL, 24°C	1.05
Mean particle size, $\mu\text{m}$	41

\* 100% a.i. basis. Compensate for purity with polymer.

**Example 18**

Following the general procedure of Example 1 a matrix particle suspension having the following composition and properties was produced.

Formulation 44
----------------

Ingredients	% w/w
Tebuconazole*	2.95
Lucite # 29	11.80
Methocel A15LV	1.00
Water	84.25
Total	100.0

Property	
% Tebuconazole	3.34
Density, g/cc, 24°C	1.03
Particle Size, microns, mean	1.9

\* 100% a.i. basis. Compensate for purity with polymer.

- 5 Formulation 43 and Formulation 44 were applied to wheat using the procedure set forth in Example 7. The data in the table below show and Fig. 14 illustrates the safety of these compounds at 10 days after planting as compared to Raxil (Bayer, Leverkusen, Germany), a commercial fast-  
10 release formulation of tebuconazole.

Rep. No.	Formulation	Rate (g a.i./ 100 kg seed)	Analytical Percent Recovery of Applied	Predicted Rate (g a.i./ 100 kg seed)	Avg. No. of Plants Germinating (out of 12)	Height of Treated Plant in cm (11 DAP)	% of Control Height (11 DAP)
14-1	ALTO 005LS	8.8	85.2	7.5	11.8	6.3	56.4
14-2	RAXIL 0.26 FS	8.8	88.3	7.8	12.0	8.1	72.1
14-3	OPUS 125 SC	8.8	62.4	5.5	12.0	2.9	25.5
14-4	41	8.8	66.3	5.8	12.0	10.2	91.4
14-5	41	17.6	86.4	15.2	12.0	9.6	85.9
14-6	41	35.2	96.8	34.1	12.0	8.7	77.5
14-7	15	8.8	75.3	6.6	11.8	9.6	86.0

667090-749260

14-8	15	17.6	82	14.4	12.0	9.3	83.1
14-9	15	35.2	94.4	33.2	12.0	9.1	81.3
14-10	77	8.8	88.8	7.8	12.0	9.4	84.1
14-11	77	17.6	78.4	13.8	12.0	8.3	73.9
14-12	77	35.2	100.3	35.3	11.8	7.9	70.2
14-13	43	8.8	73.1	6.4	12.0	10.5	93.9
14-14	43	17.6	80.8	14.2	12.0	9.9	88.3
14-15	43	35.2	95.5	33.6	12.0	9.5	84.8
14-16	44	8.8	94.7	8.3	12.0	9.7	86.4
14-17	44	17.6	69.6	12.2	11.5	9.9	88.3
14-18	44	35.2	104.3	36.7	12.0	9.0	80.5
14-19	45	8.8	64	5.6	12.0	6.3	56.3
14-20	45	17.6	63.9	11.2	12.0	4.2	37.5
14-21	45	35.2	84.5	29.7	12.0	2.5	21.9
14-22	46	8.8	78.9	6.9	11.5	7.8	69.5
14-23	46	17.6	77.7	13.7	12.0	6.7	59.5
14-24	46	35.2	93.2	32.8	12.0	3.7	33.1
14-25	UN-TREATED CHECK	0	0	0.0	12.0	11.2	100.0

**Example 19**

Following the general procedure of Example 2 a matrix particle suspension having the following composition and properties was produced.

5

Formulation 45	
Ingredients	% w/w
Epoxiconazole*	2.95
Chronopol 95	11.80
Methocel A15LV	1.00
Water	84.25
Total	100.00

Property	
Epoxiconazole* (Wt %)	3.01

Density, g/mL, 24 °C.	1.04
Ave. particle size, $\mu\text{m}$	2.80

\* 100% a.i. basis. Compensate for purity with polymer.

### Example 20

Following the general procedure of Example 2 a matrix  
particle suspension having the following composition and  
properties was produced.

Formulation 46	
Ingredients	% w/w
Epoxiconazole*	2.95
Lucite #29	11.80
Methocel A15LV	1.00
Water	84.25
Total	100.00

Property	
Epoxiconazole* (Wt %)	3.18
Density, g/cc, 24°C	-
Particle Size, microns, mean	-

\* 100% a.i. basis. Compensate for purity with polymer.

The Formulation 43 and Formulation 44 suspensions were applied to wheat using the procedure set forth in Example 7. The data in the table below show and Fig. 15 illustrates the effects of these suspensions were compared with the effect of Opus (BASF AG, Limburgerhof, Germany), a

commercial fast-release formulation of epoxiconazole. The maximum safe rate of application of Opus as a seed treatment is approximately 1 g / 100 kg seed.

5

Rep. No.	Formulation	Rate (g a.i./ 100 kg seed)	Analytical Percent Recovery of Applied	Predicted Rate (g a.i./ 100 kg seed)	Avg. No. of Plants Germinating (out of 12)	Height of Treated Plant in cm (11 DAP)	% of Control Height (11 DAP)
14-1	ALTO 005LS	8.8	85.2	7.5	11.8	6.3	56.4
14-2	RAXIL 0.26 FS	8.8	88.3	7.8	12.0	8.1	72.1
14-3	OPUS 125 SC	8.8	62.4	5.5	12.0	2.9	25.5
14-4	41	8.8	66.3	5.8	12.0	10.2	91.4
14-5	41	17.6	86.4	15.2	12.0	9.6	85.9
14-6	41	35.2	96.8	34.1	12.0	8.7	77.5
14-7	15	8.8	75.3	6.6	11.8	9.6	86.0
14-8	15	17.6	82	14.4	12.0	9.3	83.1
14-9	15	35.2	94.4	33.2	12.0	9.1	81.3
14-10	77	8.8	88.8	7.8	12.0	9.4	84.1
14-11	77	17.6	78.4	13.8	12.0	8.3	73.9
14-12	77	35.2	100.3	35.3	11.8	7.9	70.2
14-13	43	8.8	73.1	6.4	12.0	10.5	93.9
14-14	43	17.6	80.8	14.2	12.0	9.9	88.3
14-15	43	35.2	95.5	33.6	12.0	9.5	84.8
14-16	44	8.8	94.7	8.3	12.0	9.7	86.4
14-17	44	17.6	69.6	12.2	11.5	9.9	88.3
14-18	44	35.2	104.3	36.7	12.0	9.0	80.5
14-19	45	8.8	64	5.6	12.0	6.3	56.3
14-20	45	17.6	63.9	11.2	12.0	4.2	37.5
14-21	45	35.2	84.5	29.7	12.0	2.5	21.9
14-22	46	8.8	78.9	6.9	11.5	7.8	69.5
14-23	46	17.6	77.7	13.7	12.0	6.7	59.5
14-24	46	35.2	93.2	32.8	12.0	3.7	33.1

1504090-4T092200



14-25	UN- TREATED CHECK	0	0	0.0	12.0	11.2	100.0
-------	-------------------------	---	---	-----	------	------	-------

**Example 21**

Wheat seeds were coated with an aqueous suspension of the matrix particles of the present invention using the following procedure.

The following water-based film coating concentrates were used for the film coating of seeds: Blue Opacoat-AG (Colorcon, West Point, PA), Sepiret 8127 Rouge (Seppic, Paris, France), and Sepiret 2020 A Rouge (Seppic, Paris, France). Sepiret and Opacoat formulas are ready-to-use colored film-forming compositions designed for the application of thin films of biodegradable polymers, usually cellulose derivatives of natural origin.

A batch film coating system (Coating Machinery Systems (CMS) PSC-5, Ames, IA) was used to apply a precision coating to specific amounts of seed. The water-based film coating concentrates were usually diluted to a 15% w/w solids concentration with water before application. Particle formulations were usually diluted to an active ingredient concentration of 0.12% w/w and coated on seed as a separate coating (using the procedure of Example 7) or in combination with the water-based film coatings. Drying temperatures were usually inlet/outlet at 100°F / 90°F with air flows at 300 cubic feet per minute (CFM). Added coating weights were usually calculated at about 2% w/w, which provides for uniform coverage. After coating, the individual coated batches of seed were analyzed for cyproconazole content ("found a.i.").

Formulation:	47	48	49	50
Treatment:	T1	T2	T3	T4
Wheat seed	Q.S.	Q.S.	Q.S.	Q.S.
Cyproconazole @ 100% (ppm)	176, 88, 44, 11	176, 88, 44, 11	176, 88, 44, 11	176, 88, 44, 11
Found a.i. (ppm)	139, 63, 29, -	120, 50, 18, -		

Formulation:	51	Alto 05LS	
Treatment:	T5		
Wheat seed	Q.S.	Q.S.	Q.S.
Cyproconazole @100% (ppm)	176, 88, 44, 11	176, 88, 44, 22, 11	176, 88, 44, 22, 11
Found a.i., ppm (2)	156, 77, 36, -	127, 71, 32, 16, 8	129, 52, 27, 14, -

5

Q.S. = Quantity Sufficient to dilute to the required concentration.

Formulation:	29	29	29	61
Treatment:	T6	T7	T8	T9
Wheat seed	Q.S.	Q.S.	Q.S.	Q.S.
Methocel A15LV	110 ppm	-		100 ppm
Urea	-	890 ppm	-	-
Ammonium Sulfate	-	-	890 ppm	
Cyproconazole @100% (ppm)	88, 44, 22, 11	88, 44, 22, 11	88, 44, 22, 11	88, 44, 22, 11
Found a.i., ppm (1)	43, 25, 15, -			51, 17, 10, -

664050-41092600

Formulation:	30
Treatment:	T10
Wheat seed	Q.S.
Methocel A15LV	-
Cyproconazole @100% (ppm)	88, 44, 22, 11
Found a.i., ppm (1)	33, 25, 9, -

Q.S. = Quantity Sufficient to dilute  
to the required concentration.

The data in the table below show and Fig. 16  
s illustrates the safety of the suspensions at an application  
rate of 16 g active ingredient per 100 kg seed, as compared  
with Alto 005LS.

Rep. No.	Treatment	Rate (g a.i./ 100 kg seed)	Avg. No. of Plants Germin- ating (out of 12)	Height of Treated Plant in cm (8 DAP)	% of Control Height (8 DAP)
16-1	Untreated Check	0	12.0	11.6	100.0
16-2	T1	1	11.8	9.5	82.1
16-3	T2	1	12.0	9.7	83.2
16-4	T3	1	11.5	10.8	92.9
16-5	T4	1	12.0	10.8	93.1
16-6	T5	1	12.0	8.4	72.6
16-7	ALTO 005LS	1	12.0	9.1	78.2
16-9	T1	4	11.8	7.7	66.4
16-10	T2	4	11.8	8.5	73.1
16-11	T3	4	11.5	9.7	83.9
16-12	T4	4	12.0	10.1	86.9
16-13	T5	4	12.0	7.0	60.6
16-14	ALTO 005LS	4	12.0	7.3	63.1
16-16	T1	8	11.5	6.1	52.2
16-17	T2	8	12.0	6.8	58.9
16-18	T3	8	12.0	9.3	80.0
16-19	T4	8	12.0	8.9	77.0
16-20	T5	8	12.0	6.7	57.4

064090-41092600

16-21	ALTO 005LS	8	11.8	5.5	47.0
16-23	T1	16	12.0	3.8	32.8
16-24	T2	16	12.0	5.5	47.4
16-25	T3	16	11.8	8.6	74.1
16-26	T4	16	12.0	8.6	73.9
16-27	T5	16	12.0	4.8	41.6
16-28	ALTO 005LS	16	11.8	3.0	25.9

**Example 22**

In this example, the polymers used were poly(methyl methacrylate) (350,000 MW, Polysciences, Inc., Warrington, PA) or poly(styrene/maleic anhydride) (75% styrene, Sigma Chemical Co., St. Louis, MO). The organic solvent was methylene chloride (American Chemical Society analytical reagent grade). Dispersing agents used were Methocel A15LV (methyl cellulose, Dow Chemical, Midland, MI); Elvanol 51-05 (polyvinyl alcohol, DuPont, Wilmington, DE); or Yelkinol P (lecithin, Archer Daniels Midland Company, Decatur IL). Active ingredients used were epoxiconazole (technical grade @ 96.2 %, BASF) or tebuconazole (technical grade @ 98.6 %, Bayer).

All formulations were prepared by an oil-in-water (O/W) emulsion/solvent evaporation procedure. Briefly, the polymer and active ingredient were dissolved in methylene chloride at room temperature to form a hydrophobic solution (15 % solids). The hydrophobic (oil, O) phase was added to a cooled (<5 °C) 0.5 - 3.0% aqueous dispersant solution (water, W) and sheared with a Silverson Model L4R homogenizer (large hole screen, 1.5 cm.) for 5 minutes at setting #5 to form an emulsion. The organic solvent was then evaporated with stirring at ambient temperatures in a

fume hood. The resulting particle preparations were normally passed through a # 60 mesh sieve to remove large particles. These particles were examined microscopically with a Leitz Dialux 20EB microscope to check for crystals and particle morphology, and evaluated using a Coulter LS-130 particle size analyzer to determine average particle size and the number of modes in the distribution.

To assay the rate of release of active ingredient from particle formulations, an aliquot of a formulation was placed in a glass bottle at a concentration at which a released active ingredient was expected to be  $< \frac{1}{2}$  the water solubility level. A solvent was then added (water or 10 % acetone). At various intervals, the bottle was shaken (200 times at time 0, 20 times for other intervals). An aliquot was removed, centrifuged 15 minutes at 2700 rpm, and filtered through a 0.45 micron PTFE filter (after discarding the first 2 mL). Assays for epoxiconazole and tebuconazole were then carried out by HPLC.

Particle suspensions having the following compositions were produced.

**Epoxiconazole-Containing Matrix Particle Formulations -  
Composition (% , w/w)**

Ingredients	Weight % of Ingredients		
	Formulation		
	52	53	54
Epoxiconazole (100% a.i. basis)	3.00	3.00	3.00
Polymer	27.00 (a)	12.00 (b)	12.00 (b)
Methocel A15LV	-	-	2.00
Elvanol 51-05	4.00	-	-
Yelkinol P	-	1.50	-
Water	83.50	83.50	83.00



**Tebuconazole-Containing Matrix Particle Formulations -  
Composition (% , w/w)**

Ingredients	Weight % of Ingredients		
	Formulation		
	55	56	57
Tebuconazole (100 % a.i. basis)	3.00	4.50	6.00
Polymer*	12.00 (a)	10.50 (a)	9.00 (a)
Methocel A15LV	1.00	1.00	1.00
Water	84.00	84.00	84.00
Total	100.00	100.00	100.00

	Evaluation Data		
	Formulation		
	52	53	54
Loading of a.i., %	20	30	40
O/W Ratio in emulsion	3/2	3/2	3/2
Ave. particle size, mode:	9.14 $\mu$ m, bimodal	7.36 $\mu$ m, bimodal	13.48 $\mu$ m, trimodal
Init. % a.i./ % REA:	3.25/0.68	4.92/2.01	5.75/2.21

\* (a) Poly(methylmethacrylate), (b) Poly(styrene/maleic anhydride)

5

In addition, phytotoxicity of the formulations on wheat and their release rates into water and into 10% acetone solutions were determined. This information is summarized below.

067050-11032260

**Epoxiconazole-Containing Matrix Particle Formulations -  
Phytotoxicity and Release Rates**

	Formulation		
	58	53	54
	% Release of epoxiconazole, after 269 hrs		
into water	0.9	6.56	1.63
into 10 % Acetone	9.71	46.7	26.6

Safety on Wheat*			
	Formulation		
	58	53	54
25 g a.i./ 100 kg seed	96.9% (25.4 g)	66.4% (12.4 g)	92.2% (28.6 g)
50 g a.i./ 100 kg seed	91.8% (46.4 g)	20.0% (42.2 g)	75.4% (53.3 g)
Opus, 8 g/100 kg	22.5% (6.4 g)		
Control (0 g a.i./ 100 kg)	100% (0 g)		

\* Plant height as a % of the height of untreated control plants. Numbers in parenthesis are the grams of active ingredient found by assay to be on 100 kg of treated seed.

**Tebuconazole-Containing Matrix Particle Formulations -  
Phytotoxicity and Release Rates**

	Formulation		
	55	56	57
	% Release, 269 hrs		
into water	2.53	3.79	14.5
into 10 % acetone	24.9	46.2	60.0

Safety on Wheat*			
- 50 g/100 kg seed	89.7% (47 g)	78.4% (45 g)	70.3% (49 g)

664090:4703260

5

10



- 75 g/100 kg seed	83.8% (70 g)	77.3% (72 g)	68.7% (78 g)
- 100 g/100 kg seed	78.4% (95 g)	74.1% (92 g)	60.8% (99 g)
Raxil, 25 g/100 kg	40.3% (26 g)		
Control (0 g/100 kg)	100% (0 g)		

\* % of height of untreated control. Numbers in parenthesis are the grams of active ingredient found by assay to be on 100 kg of treated seed.

5           Particles having the same polymer and active  
ingredient loading (Formulation 53 versus Formulation 54)  
but using a different dispersant have much different  
release rates and corresponding differences in safety on  
wheat. The high release rate and higher initial % REA of  
10 Formulation 53 gives a product having poor safety on wheat.  
However the same loading in the same polymer processed with  
a different dispersant gives a recipe with a lower release  
rate and readily extractable active (REA) and higher safety  
on wheat. In addition, the rates of release of active  
15 ingredients are higher (and safety on wheat decreases  
correspondingly) as the loading in the particle is  
increased.

This study indicates that release rates can be changed  
by processing and active ingredient loading (concentration)  
20 in the matrixed particle. As active ingredient  
concentration increases, release rates increase likewise.  
Lower release rates tend to result in higher safety on  
wheat. When different dispersing agents are used for the  
preparation of emulsions, the emulsion quality and the  
25 release rate of the resulting particles are affected.

Poly(methylmethacrylate) and poly(styrene-maleic  
anhydride) are useful polymers for producing particles that

004090-409260

increase the safety of epoxiconazole and tebuconazole on wheat.

### Example 23

5 For this Example, the polymer used was poly(styrene/maleic anhydride) (75% styrene, Sigma Chemical Co., St. Louis, MO). All organic solvents were of American Chemical Society (A.C.S.) analytical reagent grade. The dispersing agent used was Methocel A15LV (methyl cellulose, 10 Dow Chemical, Midland, MI). The active ingredients used were as follows: the fungicide triticonazole (technical grade @ 91.8 %, Rhône-Poulenc Ag Co., Research Triangle Park, NC), the herbicide triallate (technical grade @ 94 %; Monsanto Company, St. Louis, MO), the Strobilurin 15 fungicide MON 46100 (technical grade @ 95 %; Monsanto Company, St. Louis, MO), the herbicide safener furilazole (MON 13900, technical grade @ 95 %; Monsanto Company, St. Louis, MO); the insecticide chlorpyrifos (high purity grade @ 99 %; Dow Chemical Co., Midland, MI); a morpholine-type 20 fungicide, fenpropimorph (used "as is" in the form of the 750 g/L Corbel formulation, BASF AG, Limburgerhof, Germany); a carbamoyl imidazole-type fungicide, prochloraz (high purity grade @ 99 %; Monsanto Company, St. Louis, MO).

25 Matrixed particle formulations were prepared by an oil-in-water (O/W) emulsion/solvent evaporation procedure. Briefly, the polymer and active ingredient used were dissolved in methylene chloride at room temperature to form a 15 % solids hydrophobic (oil, O) solution. This oil phase 30 was added to a cooled (<5 °C) 0.5 - 3.0% aqueous dispersant solution (water, W) and sheared with a Silverson Model L4R

664090" 4109260

homogenizer (large hole screen, 1.5 cm.) for 5 minutes at setting #5 to form an emulsion. The organic solvent was then evaporated with stirring at ambient temperatures in a fume hood. The resulting formulations were normally passed  
5 through a # 60 mesh sieve to remove large particles and then evaluated. The particles were subjected to microscopic examination with a Leitz Dialux 20EB microscope to check for crystals and particle morphology and a  
particle-size evaluation using a Coulter LS-130 particle  
10 size analyzer to determine the average particle size and number of modes in the distribution.

Test compositions were prepared and their physical properties evaluated. The two recipes used are described below. Recipe B was necessary for triticonazole because  
15 much crystal growth occurs when recipe A is used. Recipe A produces a 20 % active ingredient loading for the particles and Recipe B produces a 5 % loading.

**Recipes (% , w/w)**

Ingredients	Recipe A	Recipe B
Active Ingredient	3.00	0.75
Poly(styrene/maleic anhydride) 75:25	12.00	14.25
Methocel A15LV	2.00	2.00
Water	83.00	83.00
Total	100.00	100.00

20

Particle size analyses were carried out on the Formulation 59 and fenpropimorph recipes and estimates from photographs were used for the other recipes.

**Table 6**  
**Recipe References**

Active Ingredient	Formulation	Recipe	Ave. size (μm)
Triticonazole	60	B	~5
MON 46100	61	A	5.4
Fenpropimorph	62	A	2.7
Furilazole	63	A	~5
Triallate	64	A	~5
Chlorpyrifos	65	A	~5
Prochloraz	66	A	4.8

5        Formulation 62 showed increased safety compared to Corbel, a commercial fast-release formulation of fenpropimorph, when applied as a seed treatment to wheat at rates of 50-200 gm a.i./100 kg seed.

10    **Example 24**

Polymers used were poly(methyl methacrylate) (350,000 MW, Polysciences, Inc., Warrington, PA) and poly(styrene/maleic anhydride) (75% styrene, Sigma Chemical Co., St. Louis, MO) were used. All organic solvents were of  
15 American Chemical Society (A.C.S.) analytical reagent grade. Dispersing agents used were Methocel A15LV (Dow Chemical, Midland, MI) and Elvanol 51-05 (polyvinyl alcohol, DuPont, Wilmington, DE).

Particles were prepared by an oil-in-water (O/W)  
20 emulsion/solvent evaporation procedure. Briefly, the polymer and active ingredient used were dissolved in methylene chloride at room temperature to form a 15 % solids hydrophobic solution (oil phase, O). This oil phase was added to a cooled (<5 °C) 0.5 - 3.0% aqueous dispersant  
25 solution (aqueous solution, W) and sheared with a Silverson Model L4R homogenizer (large hole screen, 1.5 cm.) for 5

5

15

Seed Treatment Formulations

Ingredients	Weight % of Ingredients									
	Formulation									
	67	68	69	70	71	72	73	74		
Epoxiconazole*	3.00	3.00	3.00	3.00	-	-	-	-	-	-
Tebuconazole*	-	-	-	-	10.00	10.00	10.00	10.00	10.00	10.00
Polymer	27.00 (1)	12.00 (2)	27.00 (2)	12.00 (1)	40.00 (2)	15.00 (2)	40.00 (1)	15.00 (1)	15.00	15.00
Methyl Cellulose	-	1.86	1.00	1.50	1.40	1.70	1.40	1.40	1.58	1.58
Polyvinyl Alcohol	3.85	-	-	-	-	-	-	-	-	-
Water	66.15	83.14	69.00	83.50	48.60	73.30	48.60	48.60	73.42	73.42
Total	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00

\* 100 % a.i. basis.

Polymers: (1) poly(methylmethacrylate); (2), poly(styrene-maleic anhydride) copolymer 75:25 ratio.

The table below provides information regarding physical properties of the particle preparations.

**Physical Properties**

Property	Formulation									
	67	68	69	70	71	72	73	74		
% a.i.	2.94	3.01	2.96	2.93	9.39	10.13	9.89	9.98		
% REA	0.27	0.19	0.03	0.55	0.08	1.19	0.24	1.50		
t° (C.) when measured	23.7	23.7	24.2	23.0	23.3	23.2	22.9	23.2		
Density, g/mL	1.07	1.03	1.05	1.03	1.08	1.05	1.10	1.05		
Viscosity, 60 rpm, cps	3.61	2.04	3.34	1.97	19.0	4.46	25.9	4.21		
pH	7.07	4.02	3.36	6.82	3.31	3.77	6.25	5.96		

**Phytotoxicity of Tebuconazole-Containing Formulations**  
(% of Control Height)

g a.i./ 100 kg seed	Formulation					
	71	72	73	74	75	Raxil
16	-	-	-	-	-	76.3
25	-	-	-	-	95.5	-
50	82.1	69.8	89.7	70.3	89.6	-
75	84.5	64.4	83.8	68.7	-	-
100	-	-	78.4	60.8	-	-

LSD(.05) = 19.14

5      **Phytotoxicity of Epoxiconazole-Containing Formulations**  
(% of Control Height)

g a.i./ 100 kg seed	Formulation					
	MON 24531	MON 24532	MON 24533	MON 24534	MON 24555	Opus
5	-	-	-	-	-	32.5
25	93.8	91.2	93.8	83.0	96.2	8.6
50	83.4	73.3	98.0	43.3	90.5	-
75	77.9	61.4	86.8	24.3	87.9	-

Epoxiconazole-containing formulations showed much less phytotoxicity than the commercial reference, Opus.

10 Likewise, tebuconazole-containing formulations showed less phytotoxicity than the commercial reference, Raxil.

Formulation 75 and Formulation 76 were also tested as foliar treatments of soybean. At rates of 50 and 250 ppm active ingredient, soybean plants treated with

15 Formulation 75 and Formulation 76 as foliar treatments displayed substantially greater vigor than plants treated with Foliculur and Opus, particularly at the higher application rate.

The dispersant used for all of the formulations was  
20 Methocel A15LV, with the exception of Formulation 67.

664050-103260



This formulation showed better processing with Elvanol 51-05 as a dispersant.

#### Example 25

5 We evaluated particle formulations containing cyproconazole for efficacy and duration in controlling brown leaf rust of wheat (caused by *Puccinia recondita*) in greenhouse experiments. Wheat seed (cv. Fortuna) were treated with test treatments (Formulation 42, Formulation 10 15, or Formulation 77, all at 32 g cyproconazole per 100 kg seed) and Alto 005LS (at 1 g cyproconazole per 100 kg seed) and seeded in standard 4" square pots containing sterilized Dupo silt loam soil. Seeding was done at a rate of 1 seed per pot, with four replicate pots of each 15 treatment rate. Seeds were covered with approximately 2 cm of the same soil and incubated under a 12 hour photoperiod, at 50% relative humidity. Growth room temperatures were maintained at 16°C during the 12 hour light period and at 12°C during the 12 hour dark period. 20 Twenty days after planting, plants grown from treated seed were inoculated with urediospores of *P. recondita*. The inoculated plants were incubated for 24 hours in a mist tent at 20°C to allow for disease infection. Disease severity was evaluated 8-10 days after inoculation. The 25 table below and Fig. 17 show the percent of rust control in this experiment in plants inoculated 20 days after planting (second leaf stage). Disease severity in untreated control plants was about 61.3%. We observed an increase in the efficacy and duration of disease control 30 by matrix particle formulations, which permitted treatment of plants with a higher rate of the active

ingredient than would be tolerated if the plants were treated with a standard formulation such as Alto 005LS.

Formulation	% Rust Control (2nd Leaf)
42	90
15	30
77	94
Alto 005LS	25

5

**Example 26****Readily Extractable Active Ingredient (REA)**

667090:77092E50

The following method can be used to estimate the amount of free active outside the particle of the present invention active plus the active ingredient immediately extractable with water from the particle of the present invention.

10

15 Transfer an aliquot of the formulation to glass bottle. Add water shake 200 times. Immediately withdraw an aliquot of the shaken solution and filter it through a 0.45 micron PTFE filter (discarding the first 3 mL). Assay by HPLC. The resulting raw ppm value in the tested

20 aliquot must be less than half of the saturation concentration of the active ingredient assayed. If the raw ppm value is higher than half the saturation concentration of the active ingredient, the procedure must be rerun with less formulation. For example, the

25 water saturation concentration of epoxiconazole is 7 ppm at room temperature. Therefore, the maximum resulting raw ppm value in a tested aliquot of an epoxiconazole

shaken solution must be less than 3.5 ppm. The water saturation concentration of tebuconazole is 32 ppm. Therefore, the maximum resulting raw ppm value in a tested aliquot of a tebuconazole shaken solution must be less than 16 ppm.

### Example 27

#### Release Rate Assay - General Method

An aliquot of formulation is placed in a glass bottle at a concentration where released triazole is expected to be  $< \frac{1}{2}$  the water solubility level. Water is added so that the total volume is about 450 mL. The pH of the medium is maintained or adjusted using a phosphate buffer. At various intervals the bottle is shaken (200 times at time 0, 20 times for other intervals). An aliquot is removed, centrifuged 15 minutes at 2700 rpm, and filtered through a 0.45 micron PTFE filter (after discarding the first 2 mL). Assays for epoxiconazole and tebuconazole are then carried out by HPLC. If the experiment calls for an adjustment of pH during the course of the experiment, the pH is adjusted using a phosphate buffer and an aliquot is immediately removed for assay.

Many changes and modifications of the invention described in this specification will occur to those skilled in the art upon studying the teachings of this specification. All such changes and modifications which are within the spirit of the present invention are intended to be included in the claims.